**Sharing Hope Through Storytelling & Connection with Shanna Tolbert**

Transcript

**[Stan:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [Hello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Shanna:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [Oh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Stan:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [Yeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Shanna:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [I mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Stan:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [It's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Shanna:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [Yes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Stan:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [Well, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Shanna:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [I did. I definitely did.](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Stan:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [Yeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Shanna:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [Hmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Stan:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [That was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and perseverance and support of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Amy:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [This is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Kelly:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [Like Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said “Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Amy:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [Thank you, Kelly, I think Clayton, you’re up.](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Clayton:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [Thanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had Lennux-Gastaut syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Lennux-Gastaut syndrome. Since then, seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. On tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits, and he wakes up with a painful ringing in his ears. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come. We can hold them, or we can try to comfort him, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined. Behind the decline, we know that there's a very high high mortality rate associated with the Lennux-Gastaut syndrome. Death has come for our son so many times. We don't know when it's going to come for him again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that Mostyn may one day stop declining and have the opportunity to make sustainable forward progress.](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Amy:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [Thank you. I think you got us all choked up here.](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Piotr:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [So basically, I just wanted to start by saying that I want to echo Tom's word about the fact that our notions are very intensive, and this is why basically I decided we decided my wife to draw the line, and just to show you like the roller coaster we're going through with Lena and with the twins basically. But before getting there I have a feeling that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the rare-disease day. The first thing happened a couple of years ago, way before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, when my wife was pregnant, I joined Biogen. And back then, I had no idea that one of my kids is going to have a genetic condition. So, there were like some kind of signs like, you know like happening way before the actual moment that we started finding out that something is wrong with Lena. So basically, as a parent because we, our kids, our twins are our first kids. So, before that, people are going through the up and downs about the emotions that roller coaster you kind of start to feel and experience the moment you get kids is hard to describe. And you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to see them in the world. And then Christmas Eve came. And I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve, like rare-disease day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you, twins is not an easy thing to manage, then Christmas Eve came and Lena started to have in Grand Mal seizures, 30 seizures in 48 hours, so we rushed to the hospital and that was the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the milk for the second one. So that was like a huge roller coaster, and after a few days we started to recover slowly because she like made all the tests, MRI, spinal fluid. Everything looked fine, and she started to have kind of pre-diagnosis of the glute 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Didn’t show Anything basically, but then she said that the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing. It’s available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Back then it took like 5-6 weeks for some reason. After two weeks we had the result and another kind of symbolic date. We found out about the PAX diagnosis during Valentine's Day and that was like the second massive deep you can see on the slide and that's basically kind of the straight through to the depression to like you know like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look back, I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done. It’s game over completely. And looking back for us, it was at the beginning. So obviously, we were grieving and on the next slide you can see our emotion is going up again. We were grieving, but at the same time we started to act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out about my situation. People are teaching me genetics and I have a business background. So, I was trying to understand all about ASO, how it works, what is the, you know, as screening and stuff like that. So, I discovered another through basically two ways. The one way was basically Biogen employee that told me that “Hey this, there's this another thing and maybe your kid could be could get there.” And also, I very quickly connected with other parents, mainly from US and that they also told me that there is this thing that, you know, Stan decided to set up to help nano-rare patients. So, I remember another day to my wife birthday we're on the call with Wendy Chung for the first time so. These days are just haunting me all the all the time. And as you can see, we started like slowly slowing to recover and we also decided to open the research foundation because PAX2 was first described in 2018. Nothing is known about this syndrome almost. We have no idea what the mechanism of action. But basically, it doesn't really matter because you know we just want to kind of treat the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So, we started the foundation, we started to get in touch with many different parents, which are kind of calling us every night, almost every day, trying to kind of learn something from us. And then September 2022 came, so exactly one year later during Lenas first birthday, we got the information that it seems that the packs to could be the way to be treated with the ASO with the other specific approach. And when I think about n-Lorem is kind of it makes me think about the rocket as you can see here. So, the moment that we've and now it's like there's no guarantees, right. But I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the moon.](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Amy:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [Thank you, Shanna.](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Shanna:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [Good morning. I'm going to stick to my notes because I'm an emotional person anyway, and then I had my daughter Ireland and just really sent me over the edge. Thank you for the opportunity to share a little bit about my precious 8-year-old daughter Ireland. She's on the left in the middle picture with her little sister, Brooke, who is 4. The top or the bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong, and a veteran NICU nurse. I'll never forget it. She looked at me and said there's something wrong, we just don't know what. So, we go home with our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why, and she started convulsing and I had never seen anybody have a seizure before, but I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CACNA1A mutation. And so, as you've heard you, you have at this answer, but no treatment options are available. Ireland’s particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seizures she's been intubated 9 times for status, but that's the right picture. So, we spent a lot of time in ICU. We always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So, the responsibility is really on us to support her respiration and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that the air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional as she is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've had good care and we've been lucky and god is taking care of her so far, but we never know like when we're going to miss one. So, when she was first diagnosed, we were told that she was the only known person in the entire world with her particular variant, no treatment options available. She's tried a long list of anti-epileptic drugs and various other therapies. She has had epilepsy surgery and the cocktail that she's currently on seems to lessen her seizures. That is not without greatly sacrificing quality of life. She's very sensitive. I think all of our kids are very sensitive, she's very sensitive to medication side effects. And so, with the biggest for her behavioral side effects are really difficult to manage. And none of these drugs address the root cause of her symptoms, which is her CACNA1A variant, and they're really only pitiful attempts at seizure reduction. Her variant affects every single aspect of our lives. When she's not battling seizures and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed, happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see, two and a half years ago we found out that Ireland's n-Lorem application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne in Atlanta. And I don't really remember what was said during that meeting, but I remember how we felt, and we know that n-Lorem is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out for her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on CACNA1A got a contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that n-Lorem is the answer to that prayer. I just want just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications and are committed to carrying this through to treatment. I know that the knowledge gained from these pioneer families will greatly impact Ireland's experience and I'm very grateful to all of you as well.](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Amy:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [Thank you.](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Luke:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [Can I just say one quick thing? Thank you all. Adding to what Stan, in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer. That night I went to visit him in the hospital and showed him videos of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he you know, wanted to have this gift that you've given us. I told Amy that I wouldn't talk because I can't go for five minutes without crying even though I have these, but I wanted to tell you what that video meant to me.](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Amy:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll come off the stage and we'll play the video, and then we'll move to the next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's Journey?](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Luke:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [I don't think so. I mean, I think that the whole point of what we're doing is to galvanize the community of nano-rare families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So, I want to thank everybody in here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours. That's all.](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Amy:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [Thank you. Thank you. And can we get a hand for our patients?](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Narrator 1:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an ASO on YouTube. Thank you for listening to the Patient Empowerment Program podcast.](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)

**[Narrator 2:](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. Any questions can be sent into podcast@elorm.org search and Lorem on Twitter, Instagram, YouTube, LinkedIn and Facebook to connect with us. This video is hosted by Doctor Stan Crook and produced with the help of the following. Professionals. Thank you for watching.)** [n-Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect one to 30 patients worldwide referred to by n-Lorem as nano-rare. Many of these patients progress and die without ever achieving a diagnosis. This is where n-Lorem comes in. They do the impossible by providing hope, and for those that they can help, free lifetime treatment. For more information about n-Lorem or today's episode, visit nlorem.org. Any questions can be sent into podcast@nlorem.org. Search n-Lorem on Twitter, Instagram, YouTube, LinkedIn, and Facebook to connect with us. This video is hosted by Dr. Stan Crooke and produced with the help of the following professionals. Thank you for watching.](mailto:StanHello, I'm Stan Crooke. I'm chairman and CEO of n-Lorem and I'm your host for the n-Lorem podcast series. The n-Lorem podcast series is a series that focuses exclusively on the needs of patients with nano-rare mutations. It's a pleasure to welcome you all today and to welcome our special guest. And to prove that no good deed goes unpunished, we have our first repeat interviewee. Shanna Tolbert, who joined us to help manage the Q&A, has joined us again today to talk about the panel which she participated in, the patient panel. One of the themes that I felt particularly keenly out of the conversations that I had with folks there and the panel itself is just the importance of hope. That knowing that there's some group somewhere that has the potential to be beneficial is working in your behalf seems to matter so much. Is that something that you experienced, Shanna and took away from the panel as well?ShannaOh, absolutely, yeah. Knowing that there's a team of the smartest of the smart, you understand this technology working on a program for just Ireland. I mean, that's every nano-rare patients dream once you have a diagnosis and you hear that there are no treatments. I mean, to finally have that, it's a dream come true, you know, and there are no guarantees. We don't know if it'll work, but just knowing that somebody is trying and that a team is making all of the efforts possible to try to get there is so comforting as a family. And I know a lot of rare-disease families. I mean, they are out there, not only parenting and taking care of their children, but pounding the pavement to try to find a cure. People kind of take it one way or another, you know, and there's no right or wrong. But to me, the feeling that it gave me is a sigh of relief. Feeling like I can focus on Ireland, you know? Tomorrow, she does have a neurodegenerative mutation and we don't know what the future holds. And so, every day is precious. And so, for me it gave me a tremendous sigh of relief. Knowing that somebody's working on this for her and I can focus on being there for her and enjoying her good days and not missing out on the bad days when she needs her mom.StanYeah. Yeah, I think that's beautifully said and far better said than I could say. And I think the impact of hopelessness is so profound, and until you've experienced it, you can't understand it, right? As you participated in the panel and got to meet some of the other parents and so on, what would you single out as a particularly important element that came out of that of that group of caring in this case, all parents, and what they had to say and the kinds of experiences they'd had?ShannaI mean, we're in such a unique position altogether. You know, there's nobody else really in the world that can understand having this opportunity with n-Lorem. And so being able to talk to those families not only as ultra rare-disease parents, but also as being in this unique and special position and having this opportunity was very special. I've kept in touch with some families and following their stories and I have dreams and visions of us celebrating together. One day, treatments for our children and I can't wait to watch these stories unfold and follow these journeys, and then also just being able to be together and ask the real questions that are on a lot of our minds like: where is you kid in the program? How is it going? That is very helpful. And it was informative to me too. Like this is not a straight and narrow path. You know, every mutation is different, and I think the discovery process for each mutation is is very different, and it can be a windy path, and so that was very educational for me. And then also it was revealing that even, you know, the challenges that n-Lorem faced in the scientific process of finding an ASO, the bumps in the road, these stories that I was hearing from other families as that n-Lorem is totally committed to doing their very best to try and overcome those challenges and figure it out. And at the end of the day, just as you say a million times, you know, we're focused on our patients that we've accepted and doing our very best. And so, I was hearing that from other families talking about their journeys.StanIt's a lonely vigil. And I guess this is an opportunity to recognize that you're not alone, and something I really hadn't appreciated fully was. There was also an opportunity to learn a lot from the other families and to stay connected after the meeting, which was something I’d hoped, and that’s great to hear. Again, to face this alone just makes it a lot harder. Anything else that you you know particularly think about as as something that came out of the panel meeting or the meeting in general or certainly meeting all the kids and the parents and so on and recognizing that some of these families traveled a long distance with difficult travel intervening really was very touching to me.ShannaYes, me, I mean, me too. I mean the stories, even though I'm living this life, the stories are no less impactful to me when I hear them, and sometimes even more because I understand them firsthand. I think not just meeting the other families, but also, you know, sitting through the talks and having the accessibility to the speakers after the talks is not something I really anticipated, but once it was in front of me, I just appreciated it so much and I think I heard you talking on another podcast about how the professionals that showed up are, you know, top level, you know, best of the best and. It was very easy. I'm sure it's the colloquial grows it may not be so easy, but my experience at the first one was if I had a question about a talk, I could approach the speaker afterwards and, you know, clarify it. I think it's so important for families, and I know you do too. This is one of the purposes of the podcast. To really understand ASO's and how it could affect the body, and you know if an ASO is found for Ireland like I have to make the risk benefit decision, you know, to actually give it to her one day, and so the the whole thing was very educational. And then I know the n-Lorem team is always there to answer my questions, but just having the face-to-face accessibility really meant a lot to me and then also face to face being able to express my gratitude for people. I mean, I was able to walk up to team members and they have genuine tears in their eyes, you know? And just knowing and feeling how much everybody truly cares meant a lot to me. And another thing that meant a lot to me is the amount of support of other professionals and industry partners that you all have and how big of a presence they had at this meeting, I have another honest thought here as a parent? Like what if we get so far with Ireland's program and then something happens to n-Lorem or something happens to Stan and God forbid, and seeing all of the partnerships and support and momentum behind everything that you've built at n-Lorem was comforting to me, seeing that n-Lorem is not going anywhere. So, that was another big take away for me.StanWell, it's wonderful for me to hear, and certainly our plan is for the meeting to stay as intimate as it has been, and a big part I think of the pluses of that meeting was the opportunity for patients and families to interact together and then the community of people interested in doing something about this, to have the opportunity to interact in a in a much more intimate way than perhaps anyone might have expected, and you know for the first meeting, one of the things I was really worried about is that these were all busy people who get invited to 500 meetings, you know, all the time. Would they come? And I was thrilled that everybody we asked basically came and was anxious to participate. I think that speaks to the power of the mission. And so I walked away just void by the commitment of others to the mission and would hope that the other patients and parents there would feel that as well. Sounds like you did anyway.ShannaI did. I definitely did.StanYeah. Well, we're looking forward to the meeting this year. Is there anything that you would like to see out of the parent or patient panel this coming year that we didn't deliver in the meeting that we just had a year ago? Or six months ago, I guess?ShannaHmm, well. I mean, I would like to bring Ireland this time, I hope she's in a place and we're able for her to come, because the other pediatric patients that were there just, I mean, it was wonderful to see them and I you know, I missed her, and I wanted her to be a part of it. So, as far as what I'd like to see, I don't know necessarily so much from you all. But I want to bring her if she's able to make the trip this year.StanThat was one of the great thrills, wasn't it? To see the kids. And I think this next year we'll have many more adult patients as well. It's important for people to remember that this is not a set of problems that just afflict children there. We have some desperately ill adults. Some of whom are being treated now. So, we look forward to doing that. It's good, and we look forward to telling you about all the progress. So, and by all means we look forward to seeing Ireland there. I mean she's why we're there, and we'd love to do that. So, I hope people's interest in the panel itself, and the panel follows this, and to the rest of our audience, thank you for listening to this, Shanna. Thank you. It's always enlightening and motivating to visit with you, and I appreciate your good spirits and courage and and perseverance and support of of Ireland, and we look forward to seeing you in Boston in in October of this year, hopefully it will be nice weather and many, many patients will be able to join us including Ireland. Thanks everybody.HostThis is the reason why we're here, right? All of them have different diagnostics journeys, different challenges that they deal with on a daily basis, but they all have something in common that there's no therapy available right now for their loved one. You know, that's what we're hoping to change one patient at a time. And so, I'm just going to introduce everybody who's not sitting in order. So, on the end is Shanna. She is mom to Ireland. And you might have seen Shanna putting stand on the spot for our first Q&A that we did on our podcast. And so, she was great, stuck in some really hard questions, which was good. And beside her is Kelly. Kelly's mom to Connor, who is patient 001 that Stan was referring to this morning and so very happy to have you here. She came all the way from San Diego. I should mention that Shanna came from Georgia. So, like they came from all over. It wasn't just like, oh, come down the street and talk for 5 minutes. It's like, no, I'm going to fly, fly out here to participate. Luke in the middle. Father of Susanna. Susanna has actually been on treatment for a year now, and we have a video that we're going to play at the end of this panel and try not to cry all the way through it. And yeah, and then Clayton is from Tampa Bay, right? Yes, and so, we just started getting these cards. So, we're at the office, and all this like mail starts coming in and there's these thank you cards. And they're like, thank you for taking Mostyn as a patient, thank you for, you know, and we not just one, not ten, not 20 like almost 100 of these thank you cards started coming in last year, around Christmas time and so we're like we got to find who this person is, you know? So, Clayton is Mostyn’s Dad, and they're here today and I really appreciate it. And if you were here at the reception last night, you heard beautiful violin by Mostyn’s Mom. So really appreciate it. And then probably our longest journey here from Poland is Piotr. Piotr did I did Butcher it? Father of Lena, one of a set of twins. And yeah, so why don't we start with you, Kelly, and you know, turn it over to you.KellyLike Amy said, my name is Kelly and my son, he's 14 years old today. His name is Connor. You know, when I walked in this morning, I was so happy to see all of the people here today. And, you know, in 2019, I was at a conference, and I saw Stan and we were talking, and he told me he had the idea of n-Lorem, and to see what it is today, you know, n-Lorem represents our hope, my family's hope. And you know, it's our happy ending and, you know, 14 years ago, my life was very, very different. I was very naive. I thought that when people got sick, they went to the doctor, they got a medicine and, you know, most people, most patients were okay. And Connor's my second son. I was a high school English teacher at the time, and from a couple of days old, I noticed something was very off about him. He cried the majority of the time. He had trouble feeding, and even before he had his first seizure at 8 months old, we were in and out of the hospital, and he had very, thorough work, ups and all of these tests, kept coming back normal. And you know, he had so many different symptoms, seizures being the most debilitating at the time we were trialing every single medication available. And at one time, you know, he was on a dozen medications for every symptom and still deteriorating. And we were being told a lot of what I consider today, just ridiculous statements, from doctors, you know, take your son home and love him while he's still here. We don't know what's wrong with him. And I was obsessed with getting a diagnosis. I thought if we just got a diagnosis, there would be a treatment available. And, you know, I was flying my son all over the country. And when he finally got whole exome sequencing and he got a diagnosis, it was an apology. It was your son has an SCN2A mutation. I'm sorry. We don't know much about it, and we have nothing available to offer you. And it was devastating. I started with scientists at USD and just started calling scientists in the area trying to find someone that knows something about this disease, and you know I'm a parent. I have three kids at home, one in and out of the hospital, and I'm being told that if you want this disease studied, you're going to have to fund it yourself. You're going to have raise money; you're going to have to find scientists, and to make a very long story short, I have 5 minutes, I ended up starting a biotech company, and I worked for years on a molecule that I thought was going to help my son, and our scientist a couple of years into that called me and said \“Kelly, I'm so sorry, but Connor is not a candidate for this molecule. His mutation is very unique. It's mixed function. Connor's going to need a little specific knockdown. He's going to need his own ASO\” Who is going to make a drug for one child. And it was the most devastated I'd been in this entire process. A few months later, I was at the Tides Conference in San Diego when I was listening to Stan speak on SPINRAZA, and I went up to say hello, and I asked him what he was doing, and he said he has an idea to start a foundation devoted to n-of-one patients where they have very unique mutations and to use ASO's and it was like almost the twilight zone for me. It was exactly to a tee what I thought my son needed and I emailed him a few days later, and I went to meet with them, and I brought our scientist and another parent. And we looked at all the science of my son's mutation and he thought that there was a potential that this could help him. And as soon as it became available, I applied to n-Lorem, and were patient 001 and. You know it's been a really challenging path, but what n-Lorem represents today, I mean, my son, his life's roller coaster, it's up and down. He has good days and not so good days. But he's going to be diagnosed or treated with an ASO this year. And I'm so grateful that my son’s life, one child, there is a team of scientists and doctors and donors, all for my son. So, it's a tragic diagnosis, but it's also really exciting times for genetics and the potential of, you know, what's possible.HostThank you, Kelly, I think Clayton, you’re up.ClaytonThanks for your interest in our son's journey. Mostyn is our only child. He was born precisely on his due date by natural birth following a healthy pregnancy. My wife, his mother, is extremely talented. She was a professional violinist and toured with Rod Stewart, Andrea Bocelli, David Navarro, Tommy Lee, to name a few. Her mother was a model. Her father was a professional football player, played in the NFL, Canadian Football League, and American Football League. And he currently holds the record for the longest punt in the world. My father was a professional golfer for a little while and then I'm not sure what happened to me. But Mostyn, Mostyn clearly has some rare jeans, and unfortunately one of those jeans has a severe, you know, very unfortunate misspelling. He's the only known case with his particular variant on a gene called KCNV1, and that variant causes him to have some severe medical challenges. When Mostyn was four, he had floppy wrists and kids started making fun of him. Adults started making fun of him, and we tried everything we could. You know, kinetic tape, TENS units, massage, physical therapy exercises. Nothing seemed to work. And then one day I came home with a baseball glove. We started playing catch and Mostyn has been wearing has been wearing a glove, sorry, Mostyn had been wearing a glove every day for the past eight years and he is falling in love with baseball and his wrists are no longer floppy. Sorry, when he was five years old, he had been working really hard, he could say nearly 100 words and he was, is able to run, is able to climb stairs. He was able to swim, and he could dance like Michael Jackson. He was out of control. He was so fast. And then on December 16th, 2031, 2031, right, I  don’t know what's going to happen on 2031. I hope we're going to make it there, but 2016 on December 31st, 2016, he suffered his first very violent tonic-clonic seizure and within a few weeks he is having four different types of seizures and as many as 30 tonic-clonic seizures a day. He knew it being hospitalized in Orlando and the third day we were there, a doctor came into his room and wrote LGS on the board and she explained to us that our son had  syndrome. I asked her what that meant, and I asked her what it meant for his life expectancy, and she just began to cry and I'm thinking this must be bad and she left the room before she'd come back in. Unfortunately, baseball gloves cannot cure Linux distress syndrome. Since then, our seizures have stripped our some visibility to walk at times. His ability to eat, his ability to swallow. He relies on a feeding tube. Sorry on tough days like today he convulses over and over. His oxygen level drops, he turns blue, he chokes, he vomits and he wakes up with a painful ringing in his ears and. He loses his balance, his ability to walk, and he gets very scared of the next seizure to come from. We can hold them, or we can try to comfort them, but we can't protect them from the next seizure. And unfortunately, the anticonvulsants have not been able to suppress his seizures fully either, and they come with a lot of side effects. They can suppress his his heart rate, his blood pressure, and his breathing. They're so strong, it's almost like he's been in a trance for the past seven years. And sometimes we look back at videos of things our son is able to do before seizures, and it's really sad watching how much has declined behind the decline. We know that there's a very high high mortality rate associated with the next pistol syndrome. Death has come for our son so many times. We don't know when it's going to come from again. I can give you countless examples of how hard Mostyn’s worked and his relentless efforts, of our efforts, and of his amazing doctor's efforts. But what matters more is this. For the past seven years, we've been using medications to manage symptoms, and Mostyn has been declining. We are so grateful n-Lorem has accepted his case. The work that n-Lorem is doing gives us hope that must may one day stop declining and have the opportunity to make sustainable forward progress.Speaker 3Thank you. I think you got us all choked up here too.Speaker 4So basically I just wanted to stop by saying that I want to echo Tom's word about the fact that our notions are very intensive and This is why basically I decided we decided my wife to draw the line. And just to show you like the roller coaster we're going through with, with Lena and with the trees basically. But before getting there I have a feeling that that as this is overall kind of haunted me well before that, so you wouldn't believe that my passport that I got into us with was issued on the 28th of February. As you know, this is the disease day. The first thing in it happened a couple of years ago, a while before, you know, I found out that we're going to have twins. And then and then 2 1/2 years ago, where my wife was pregnant, I've joined Biogen. And back then, I had no idea that one of my kid is going to have Ultra ultra genetic condition. So there were like some kind of signs like, you know like happening way before the actual moment that that we started finding out that something is wrong with Anna. So basically as a parent because we, our kids, our twins are our first kids. So before that, people are going through and the up and downs. About the emotions that roller coaster you you kind of start to feel and experience the moment you get kids is hard. To. Describe and that was you can see all the way up the moment that the twins, the twins, were born in the September 2021, everything was going well. We're like happy and just waiting for the kids to, you know, just to look like just to see them in, in, in, in in the. And and then and then Christmas Eve came. And yeah, I have some kind of, let's say, strange connection with this kind of dates, like Christmas Eve out. Like this day on the 28th of February, my passport and the moment we started to recover from the sleepless nights because I can tell you. Queens is not an easy thing to manage. The Christmas if came and Lena start to have grandma starts the Politicus 30 series in 48 hours, so we rushed to the hospital and that was our the first massive hit. And something that maybe it's not like easily seen on the slide is that there was a. Second baby. So, like my wife, she was in the hospital like having that kind of experiencing the seizure, like every hour and a half, while there was a second one at home. And I was like kind of single parent before we kind of started to basically take care of decisions of Lena. And I remember myself. It was during COVID time COVID times, I was rushing between home and the hospital to get the milk so that I was basically kind of entering hospital illegal during COVID times just to get the meat for the second one. So that was like a huge cost and. After after a few days we started to recover slowly because other doctors she like made all the tests, MRI, spinal fluid. Everything looked fine and she started to have the she started to have kind of pre diagnosis of the glute. 1. But then a couple of weeks later, the gene panel ruled out gene panel did this. Did it show? Anything basically, but then she said that the the thing and I want, I want to basically like echo your words. There was like one last thing we can try which is called whole exome sequencing is available commercial. But obviously I think to the fact that we both worked in the corporate world, we were able to kind of you know afford that over basically overnight. And we're like, you know, we're like, still waiting for the for the results. Normally it took it back then it took like 5-6 weeks for some reasons. After two weeks we had the result and another kind of symbolic date. We found out about. We found out we found out about the PAX diagnosis during Valentine's Day and. And and that was like the second massive deep you can see on the slide and that's basically kind of the the, the, the straight through to the depression to like you know like like like there are like many things like going to your head. However, now if I look back and if you can go to the next one if basically if I look if I look back. Is. I had the feeling that that was the kind of the starting point, so looking back like, you know, more than a year ago, it's like, you know, at some point you think it's like it's done, it's getting over completely and looking back for us, it was at the beginning. So. So obviously we were grieving and on the next slide you can see our emotion is going up. Again, we are grieving, but at the same time we started to act act quickly. I was always open, always vocal, always transparent. So countless people at Biogen found out found out about my my situation. People are teaching me genetics and I have business background. So I was trying to understand all about ASL, how it works, what is the, you know, as screening and stuff like that. So I discovered another through basically two ways. The one that the one way was basically. An employee that told me that hey this, there's this another thing and maybe your kid could be could get there. And also I very quickly connected with other parents, mainly from us and that they also told me that there is this thing that, you know, Stan decided to to set up to help none of their none other patients. So I remember another day another another day to my wife birthday we're on the call with Randy Chang for the first time so. These days are just haunting me. All the all the time, and as you can see, we started like slowly slowing to recover and we also decided to open the Research Foundation because PAX two was first described in 1018. Nothing is known about this syndrome. Almost. We have no idea what the mechanism of action. But like basically, it doesn't really matter because you know we just want to kind of treat the the, the, the, the, the patient without knowing fully and understanding fully what is causing the disease. However, we wanted to kind of give back something to the community. So we started the foundation, we started to get in touch with many different, many different, many different parents, which are kind of calling us every night. Almost every day trying to kind of learn something from us. And then September 2022 came so exactly one year later during during Clannad's first birthday, we got the information that it seems that the packs to could be the way to be treated with the ISO with the other specific approach. And when I think about the Lauren is is kind of it makes me think about the rocket. As you can see here. So the moment that we've we've and now it's like there's no guarantees, right. But we I have a feeling that we are basically part of a big group building the rocket and maybe at some point we'll be able to get in and just, you know, take our daughter and just fly to the.Speaker 3Thank you, Shanna.ShannaGood morning. I'm going to stick to my notes because I I'm an emotional person anyway, and then I had my daughter Ireland and just really sit me over the edge. Thank you for the opportunity to share a little bit about my precious 8 year old daughter Ireland. She's on the left in the middle picture. With her little sister, Brooke, who is 4. The top or the? Bottom left picture is Ireland shortly after birth, when she was taken to the NICU, she was they called her a jittery baby and she had a couple of episodes of apnea where she just randomly stopped breathing and they did a million tests. Couldn't really find anything wrong in a veteran NICU nurse. I'll never forget it. She looked at me and. Said there's something wrong, we just don't know what. So we go home with our our new baby and trying to enjoy her. And she's a little bit delayed. The talents of the developmental milestones and then at six months old, she was sleeping on my chest because she was a terrible sleeper. We now know why and she started convulsing and I had never seen anybody have a seizure before, but I I knew immediately she's having a seizure, so we call 911 and. Few more seizures followed from there, and our incredible team at Children's Healthcare of Atlanta immediately did genetic testing and so we got a quick, pretty quick diagnosis of the CCNA 1A mutation. And so as you've heard you, you have at this answer. But no treatment options are. Whole islands, particular variant is neurodegenerative. It causes intractable epilepsy, ataxia, global developmental delays, cognitive impairment. She has an autism diagnosis and severe hemiplegic migraines, and her seizures are all or nothing. She's not having daily seizures, but when she does, they're always status epilepticus. She requires multiple rescue drugs. She has a very unconventional rescue protocol because none of the FDA approved rescue drugs have ever stopped her seed. Years she's been intubated 9 times for status, but that's the right picture. So we spent a lot of time in ICU, we. Always carry an emergency bag everywhere we go with her little mobile pharmacy and ambu bag because she also stops breathing, turns blue and it's status, so this seizures not stopping. She's blue. So the responsibility is really on us to support her respira. Ocean and she has a little nasopharyngeal airway, which is the little tube that goes in her nose to lift the tongue off the back of her throat so that. The. Air can get in, so thankfully thanks to her care team in Atlanta, we do have this very aggressive rescue protocol. I think it's the only reason she's as functional. She is. But we live in constant fear of the next big neurological event being the one that changes her forever. And I think we've been we've had good care and we've been lucky and God is taking care of her so far, but we never know like. When we're going to miss. 1. So when she was first diagnosed, we were told that she was the only known person in the. Entire world with. Her particular variant, no treatment options available. She's tried a long list of anti epileptic drugs and various other therapies she has. She said epilepsy surgery and the cocktail that she's currently on seems to lessen his seizures. That not without greatly sacrificing quality of life. She's very sensitive. I think all of her kids are very sensitive to medical. She's very sensitive to medication side effects. And so with the biggest for her behavioral side effects are are really difficult to manage. Ireland. Let's see. And none of these drugs address the root cause of her symptoms, which is her calc and 1A variant. And they're really only pitiful. Attempts at seizure reduction. Her variant effects every single aspect of our lives. When she's not battling seizures and and recovering and medication side effects, we do get a glimpse of what I call like the real Ireland and she's bright eyed. Happy, giggly. She's funny. She's got a great sense of humor, and she's really just an Angel. And I know I'm her mother, but she is. Let's see. 2 1/2 years ago we found out that Ireland's emporium application was accepted. This opportunity is what every nano rare, patient and family dreams of. In August of that year, we had the opportunity to sit down with Stan and Roseanne. In Atlanta. And I don't really remember what was said during that meeting, but I remember. How we felt. And we know that in Lauren is 100% committed to doing the very best they can to find an optimal ASO for Ireland. For years I felt like the burden of trying to figure this out. For her was entirely on my shoulders. I googled till my eyes hurt. I contacted research. Anybody who had published on talking when I got it, you know, contact from me. And it's such I can't tell you the tremendous sigh of relief knowing that somebody else is kind of picking this up for her and carrying carrying the torch to try to fix it for her. Our entire family has been praying since her diagnosis for healing for her, and it is our hope that in Lauren. Is the answer to that prayer I just want. Just to close, take a minute to acknowledge the initial patient families who and their care team and the doctors who have supported their applications. And are committed to the to carrying this through to treatment. I know that the knowledge gained from these pioneer families. Will. Greatly impact Ireland's experience and I'm very grateful to all of you as. Well.Speaker 3Thank you. Yes, yes.Speaker 7Quick thing. Thank you all. Adding to what? What? Stan in the very beginning, you saw a video of Susanna standing up. That was the first time she stood in three years. She had lost the ability to stand. And at the time my father was dying of cancer and. That night I went to visit him in the hospital and showed him. Video of Susanna standing up for the first time in so many years, and he died a few days later, and it was almost as if he. You know, wanted to have this gift that you've. Give us some. I told Amy that I wouldn't talk because I can't go for 5 minutes without crying. You know, I have these, but. I wanted to tell you what that video meant.Speaker 3And a thank you for sharing it with us and we could share it with the community. I think you know, at the end of this panel, we have another professionally produced video that Biogen has done for us about Susanna's journey through her treatment. And I was really going to play it while we're all up here. But I think maybe what we'll do is we'll. We'll come off the stage and we'll play the video and then we'll move to the next next section before we do that, Luke, is there anything else that you would like to say before we play Susanna's?Speaker 7I don't think so. I mean, I think that the whole point of what we're doing is to galvanized the community of nanowire families. And if we all don't put our shoulders behind that, be it with resources or awareness or whatever, then you know, it's just going to be more difficult. So I want to thank everybody. In here for putting your shoulder behind that galvanized community and to continue doing that, it means the world to families like ours and. That's all.Speaker 3Thank you. Thank you. And can we get a hand for? Mr. chair.Speaker 8For those listening to the audio version of this podcast on Spotify, Apple Podcasts, and most other streaming platforms, you can watch Suzanna's story treated with an ASO by clicking the link in the description or by searching Susanna's story treated with an SO on YouTube. Thank you for listening to be patient Empowerment Program podcast.Speaker 9And Lorem is a nonprofit committed to discovering and providing personalized, experimental treatments for free, for life to patients with genetic diseases that affect 1 to 30 patients worldwide. Referred to by Ellorum as nano rare, many of these patients progress and die without. Ever achieving A diagnosis. This is where Enorm comes in. They do the impossible by providing hope, and for those that they can help free lifetime treatment. For more information about end Lorem or today's episode, visit enorm.org. 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