**CROs and Their Role for Nano-rare with Jamie Macdonald**

# **Transcript**

Narrator

Today's episode is brought to you by Parexel. Parexel is among the world's largest clinical research organizations, providing the full range of phase one to phase four clinical development services to help lifesaving treatments reach patients faster, leveraging their breadth of clinical, regulatory, and therapeutic expertise. Parexel’s team of more than 19,000 global professionals works in partnership with biopharmaceutical leaders, emerging innovators, sites and organizations like n-Lorem to design and deliver clinical trials with patients in mind. This increases access and participation to make clinical research a care option for anyone, anywhere. The company's depth of industry knowledge and strong track record gained over the past 40 years is moving the industry forward and advancing clinical research and healthcare's most complex areas like rare disease. With the people, insight, and focus on operational excellence, Parexel works with heart every day to treat patients with dignity and continuously learn from the experiences so every trial makes a difference.

Stan

Hello everyone, it's Stan Crooke. I'm chairman and CEO of n-Lorem, and I'm your host for the n-Lorem podcast series. Today, I'm very pleased to have a colleague, Jamie Macdonald. Jamie is a CEO of Parexel, and we're going to spend some time talking about what Parexel is, and how important what Parexel does is to our ability to help patients with nano-rare diseases. Jamie, welcome. It's great to have you.

Jamie

Stan, delighted to be on and obviously delighted to work with n-Lorem as well.

Stan

Well, given the fact that you're Scott, I have to do this. I'm sorry, but do you play bagpipes, and do you eat haggis?

Jamie

No to the bagpipes, but absolutely yes to haggis. A little bit of my upbringing. So, I've been in the states a long time, but I'm still lucky enough that I get to go home, see family, eat haggis, listen to bagpipes when other people play them.

Stan

Yeah, well, more power to you. I tried it once and I thought I was going to gag for the rest of my life, but okie dokie. And surely you play a lot of golf when you can.

Jamie

That was definitely one of the things growing up. It was great to grow up in Scotland despite the weather. Golf is a national pastime, as you would guess, and being here in the states now there's a lot of opportunity, and better weather.

Stan

A lot better weather. So, I know you grew up in Scotland. Did you grow up in Edinburgh directly or outside?

Jamie

Outside. So, my background is my father was a farmer. His father was as well. My grandfather on the other side served in the Royal Air Force, so he was a military man. But I grew up in a farm and my two brothers still farm, but I ended up in Edinburgh at university. I went to Heriot-Watt University and studied economics, and then worked in Edinburgh for quite a long time before being relocated with work here to North Carolina, and I've been here almost ever since. I had a couple of years back in the UK.

Stan

Quite a transition just in geography.

Jamie

It's relatively easy. It's a common language. I think the cultures are different, but the common language definitely helps.

Stan

And in the South, you've got a lot of residual effects of Scottish music on the music in the South, right?

Jamie

Yeah. And sort of culture, I think. The Scots migrated probably from the 17 and 1800s, came into the sort of northern side of the states, and Canada. Obviously, Nova Scotia is New Scotland and then as you came in through Maine, a lot of them tried to avoid the heat in the South and stayed up in the Appalachian Trail. So, you've got Highland games still in parts of North Carolina, and then you have town names like Aberdeen that are very much Scottish names. So, there's quite a bit of Scottish heritage here.

Stan

Yeah, I had the distinct, boring event of watching log, tree throwing or whatever. Whatever you call it.

Jamie

Yeah, tossing the caber. A strange name, but yeah, essentially tossing trees.

Stan

Well, anyway, we could talk sports for a while, but we probably ought to move on. So, you obviously grew up on a farm, and you did your degree in economics. Those are both about as far afield from the practice of medicine and the delivery of medicines as one could imagine. Tell us how you migrated from nice sensible business principles to the sort of odd process of drug discovery and development.

Jamie

Yeah, and it was serendipity. It's an unusual way to come into the industry, but I came in on the finance side. So, after I did my degree in economics, I'm a chartered management accountant, so more the business side of finance. And I was lucky enough, I got a job in Edinburgh for a company called Syntex which no longer exists. It was acquired by Roche back in 1994. They produced a very good analgesic compound. So, many people in the US would know it as Aleve, but it's naproxen sodium. So, I joined Syntex back in 1994 on the finance side. It was an integrated development site, so it had everything from preclinical manufacturing, pharmaceutical sciences, regulatory affairs, and clinical. So, I got a great learning even from the finance perspective for about four or five years in Edinburgh before coming to the states. So, it was a little bit of serendipity on the finance and accounting side, and I stayed in that world really for about eight or nine years before moving across to the operations side, initially on the early development side. So, as you would know, it's preclinical pharmaceutical sciences, labs, phase one, and then progressed into the clinical and project management world.

Stan

Well, it is an interesting journey. I suppose those of us in the industry always know this and assume it, and that is many come into the industry with the idea that they'd like to do something of value with their life, and with their work, and making a drug is certainly that. And others sort of find their way to it after entering the industry. When did it sort of hit you that you were privileged to be doing something that could matter to patients.

Jamie

Yeah, it was sort of interesting for me, and sort of my late high school, as you would call it in the US, I concentrated on three subjects, one was economics and obviously that's where I went and did my degree. The other two were actually biology and chemistry. So, I actually had a little bit of that background prior to going off to university. I think it was pretty obvious early on how impactful the industry was in terms of creating new and better therapies to treat patients. I think for me, the really clarifying point of time, I lost both my parents to cancer when they were fairly young. So, my father was 60, my mother was 63. And I was really just starting to get involved from moving from finance to operations, understanding the drug development process from discovery, and preclinical, into clinical studies, and how long and expensive that process was. And at the time, as you know, it would take as many as 12 to 14 years to go from discovery to market authorization, and the costs were significant. Certainly, back in the 90s, probably as much as $2 billion, and in today's dollars it may be as many as $4 billion to go from discovery to market authorization, prior to, obviously, getting into personalized medicine and having platforms that allow us to be more efficient and more effective at developing new drugs.

Stan

So, did you move to North Carolina with Syntex or Roche? It was Roche by that time, I think.

Jamie

It was Quintiles, so it was quite interesting. Roche already had substantial capabilities in the UK, Welwyn Garden City, and London, when they acquired Syntex, they acquired the Maidenhead facility in the UK and then Edinburgh in Scotland. And they divested that site and about 300 people to what was a small CRO at the time called Quintiles, which is now IQVIA. And I spent a long time with them, 16 years, and was very fortunate. I spent time in the UK, US, back to the UK, back to the US, and went from finance to operations, initially on the early phase side and preclinical, but then into clinical and project management, which I think most people know is the real clinical trial space. That's where you start to get involved more with customers, study design protocols, engaging investigators and physicians, and ultimately, obviously bringing patients into the clinical trial process through consenting and screening for trials that they're eligible for.

Stan

And you use the term CRO that many are not familiar with. It means contract research organizations of course. And there are a wide range of different types of services that are provided to the industry. And all those services can in one way or another be considered contract research organizations. But you were in a particular sort of sub-slice of that CRO industry and on the clinical side, is that right?

Jamie

It is. We provide support really for that first in human study, which is as you know, but others might not know is generally in healthy volunteers, in many instances, all the way through the necessary patient trials to prove out safety, which is critically important, and then efficacy of new therapies, and then at large enough scale obviously to be statistically significant in order to support registration and market authorization. So, we're really in that clinical space, but as you say, we provide services from clinical operations, project management, logistics, regulatory. It's a complex global environment to run clinical trials and we have 20,000 people situated around the world. We have more people in Europe than we have in the North Americas. We have more people in Asia than we even have in Europe as well. So, it's a truly global company, and the clinical trial environment is truly global, but supporting companies obviously like and n-Lorem or Ionis or others who need those global capabilities, and scale, and experience that we bring. So, we're on the service side of the industry, we don't own products. We don't necessarily market or sell products, but we provide all those services.

Stan

And I think one of the goals out of this conversation is to help people understand how really complex and challenging clinical trials actually are, and of course, if you have a very large clinical trial, you need to identify multiple physicians and sites that are capable of conducting the trial and taking care of the patient. And then you have to manage collecting all the data, make sure it's done right, and all that. Parexel is one of the larger clinical research organizations. I don't know if you're two or three or four, but somewhere in there, I suppose. You want to just talk to folks about the challenges of actually getting a big trial started?

Jamie

Yeah, it's a very complicated process and it sort of really starts with identifying the patient population. I think all of us look at patients, and disease, and etiology, and how new therapies might benefit those patients. Obviously, everybody would like to create curative therapies. I think sometimes people think that that's the case, but actually there's a whole spectrum of, obviously, prevention. So, think about vaccines. There is a limited number of curative therapies that completely resolve diseases for patients and that's obviously exciting work, but there are trials that are designed to alleviate symptoms, slow the progression of disease, and I think you have to understand the patient, the etiology, and the movement of disease, and how those new therapies potentially target those diseases, and then focusing in on where are you going to find those patients? Where are you going to find physicians that treat those patients? How do you engage in a contracting process, establish their credentials and their experience necessary to run those clinical trials, and then obviously protecting the patient throughout? I think the whole system is really designed to ensure the welfare and the rights of the patient are protected throughout. It's global, so the regulations, even though they're harmonized at a global level through what is called ICHGCP. So, the International Conference and Harmonization Good Clinical Practice, they do vary country by country. So, we're trying to navigate in some trials as many as 30 or 40 countries. Quite often, hundreds of sites and contracts, but then logistics. How do you get drug supply, labs supply, consumables to those sites? The documentation processes, as you know, is significant. Essentially, the construct of a clinical trial has to be recreated from all the documents and data that we gather throughout that trial, so that bodies like the FDA and other global agencies can come in and audit the conduct of the trial in line with the Protocol and GCP. So, it's a massively complicated process. I think people understand it relatively simply, but actually the logistics and documentation and process and rigor and audit is significant, and quite rightly so.

Stan

Yeah, it is. No wonder it's so costly. No wonder it's so time-consuming. One of the notable features of Parexel is its experience, strength, focus on rare and ultra-rare disease, and now of course into single patient trials, or I don't think we should call them. Every exposure of an experimental agent is an experiment in my view, but obviously they're not trials in the same way that an FDA trial would be to gain approval. How did Parexel happen to gravitate toward that rare end of the spectrum of diseases?

Jamie

Well, it's quite interesting. As you know, the industry historically was designed and served sort of larger disease populations. That was always the case. I think the progress that particularly has been made on the discovery and early development side has allowed us to sort of personalize some of these medicines. So better understanding of biology, better understanding of genetics, the whole Human Genome Project has been important for drug research. And that's allowed companies to look at the rare, and even nano-rare space, where it's become more feasible with the support of the regulators. I think agencies like the FDA, and EMA in Europe have enabled the research to target what has been quite an underserved patient population, where there was, being rare disease, maybe less than 1000 patients globally. And then into the nano-rare spaces, you know, which is maybe less than 20 or 30 patients globally, they've quite often been underserved because the historic process cost and timelines didn't really allow for the more commercial or economic based research to support those patients. And I think obviously with n-Lorem, and the foundation, but I think others in the space as well have realized that we can develop really impactful therapies for patients, particularly in the younger populations, adolescents and pediatrics, and we can build infrastructure and support that allows us to conduct, as you say, these experiments or trials that really can be life changing for those patients. So, it's a sort of motivation of the company as well as obviously a business decision.

Stan

You bet. It's called helping patients, right? And of course, I've spoken many times that what n-Lorem is doing is industrializing the process of providing for free, for life, personalized ASO treatments to this extraordinarily rare patient population. Many of our patients really, so far as we know, are unique. That patient and that patient only has a mutation that is expressed in that patient. And one of my goals was to establish the infrastructure that would support all that because we look out and we plan to be treating many thousands of patients. That's a tough, tough task. That's hundreds of individual trials at the same time. And as you know, we talked to several clinical research organizations. Ultimately you and I decided that Parexel and n-Lorem were an appropriate combination and an appropriate business investment and support from your perspective, and an important decision on my part to put our patients to some extent in your hands as well. And not every clinical research organization was interested, but Parexel was immediately and keenly interested. How come?

Jamie

I think it fits with the mission of, obviously we're a commercial organization, I think we do work, we are here to basically serve our investors on board, but I think sometimes you have another mission, which for us is really to understand how we can better serve patients, and I think the work that you're doing just sort of highlighted our sort of patient first mentality and our sort of we care approach. And it's been quite interesting, we run hundreds of trials globally for a wide swath of the industry, if you want to call it that, but we internally get a lot of really positive feedback for the work we do without n-Lorem. It becomes quite personal for, not just the team that's working with your team, but I think the wider Parexel organization appreciates that we're working with you to bring clinical trial options to patients that might not otherwise be served by the industry. I think that's really good work. We do good work all of the time in terms of important work, but I think when we can do it in a way that it might not otherwise get done, I think that's rewarding for us and our teams, not just the ones working with n-Lorem.

Stan

Yeah, that's very nice to hear. I think we are simply a tangible expression of the heart of our industry. And our partnership with Parexel is vital to our ability to meet our mission. And as you know, in somewhere around two weeks in September here, we filed four INDs. INDs are the documents that they have to provide to the FDA to gain approval to expose a patient of any sort to an experimental agent. And we've been working with your team to be sure we were ready to take good care of those patients and to acquire all the knowledge that we could acquire as we treat those patients and I know it was exciting for us. I imagine it was pretty exciting at Parexel too, wasn't it?

Jamie

Yeah, very much. And we share that news with the organization. It's something to be very proud of. It's a complicated process as you've said. An IND takes a lot of work. It's a lot of effort. Our teams work well together, so I think on our side, obviously Angela is really a great resource, but yourself and Sarah on that n-Lorem side have worked well together. The process that you have for identifying patients that you could potentially treat is thorough and robust, and I think that's important as well. But it includes stakeholders on the manufacturing side. I think the agency has been very supportive from what we've seen. It's nice when it sort of comes together. It's very rare that you see that number of stakeholders that well aligned on a particular mission to support, not just the patients for us, I think it's an extension to the family and the caregivers and others. This is potentially life changing for the patient, but for their own family and their own ecosystem. And that's really rewarding work from just an emotional standpoint. If you can't be empathetic in this industry, you're probably in the wrong industry.

Stan

Yes, I think if you don't care about the patient, eventually you'll lose your way and do something that harms the industry. We've seen that happen. And so, it is wonderful for me. Every partner we have says pretty much what you say. It's been an incredible benefit and employee engagement and commitment because it is the true expression of why many people come to work every day in this industry, and that I think, is why we've gotten so much support and it is quality of the mission and the need for the mission. And we couldn't do it without you. So, thank you and all your team for that. We'll be asking for more.

Jamie

And we're here to support. I think that need that you reference is critically important, and I think the industry sometimes has sort of overlooked the ultra or nano-rare patient population. And I think what you're doing, and n-Lorem is doing is showing that that is possible. There are structures and mechanisms and platforms that will allow the industry to identify diseases that we can treat. The technology is there. The platforms are there, but there has to be a willingness to do the work and fund the work in order to benefit those patients. And I think this model is one that obviously, as n-Lorem grows and extends, will support patients, but hopefully we see the model replicated elsewhere.

Stan

Hope so. So, it's creating the path and then having others follow the path. That is where all the leverage comes from. Well, Jamie, it's been a delightful chat with you as always, and I'm absolutely confident that our listeners have gained a good bit of information. And so, folks who are listening, Parexel is one of the vital elements of the process. Without it, we can't do what we do and do it right. Is there anything I have forgotten to ask you that you'd like to say, Jamie, before we sign off?

Jamie

No, Stan, it’s always a pleasure to speak to you and work with the team. I think we have regular dialogue, as you know, outside of these podcasts and it's great to be connected. And I think that's what the industry is about. It's making connections across all the stakeholders, and I think helping people understand there's a lot of good people in this industry trying to do important work. And when you get it all aligned well, we can do great and meaningful things, and that's what keeps us all motivated and keeps us all busy.

Stan

Well, thank you for that. And with that, Jamie, thanks again, and thanks everyone for listening, and we'll be talking again.

Jamie

Pleasure. Thank you everyone.

Narrator

Today's episode is brought to you by Parexel. Parexel is among the world's largest clinical research organizations, providing the full range of phase one to phase four clinical development services to help life saving treatments reach patients faster. Leveraging their breadth of clinical, regulatory and therapeutic expertise, Parexels team of more than 19,000 global professionals works in partnership with biopharmaceutical leaders, emerging innovators, sites, and organizations like n-Lorem to design and deliver clinical trials with patients in mind. This increases access and participation to make clinical research a care option for anyone anywhere. The company's depth of industry knowledge and strong track record gained over the past 40 years is moving the industry forward and advancing clinical research in healthcare's most complex areas like rare disease. With the people, insight, and focus on operational excellence, Parexels works with heart every day to treat patients with dignity, and continuously learn from the experiences so every trial makes a difference. n-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 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. Please rate and review the podcast on Apple, Spotify, or wherever you listen. This truly helps us climb the charts and allows others to find the show. This podcast is hosted by Dr. Stan Crooke. Our videographer is Jon Magnusson of Mighty One Productions. Our producers are Jon Magnusson and Kira Dineen of DNA today. Thank you for listening.