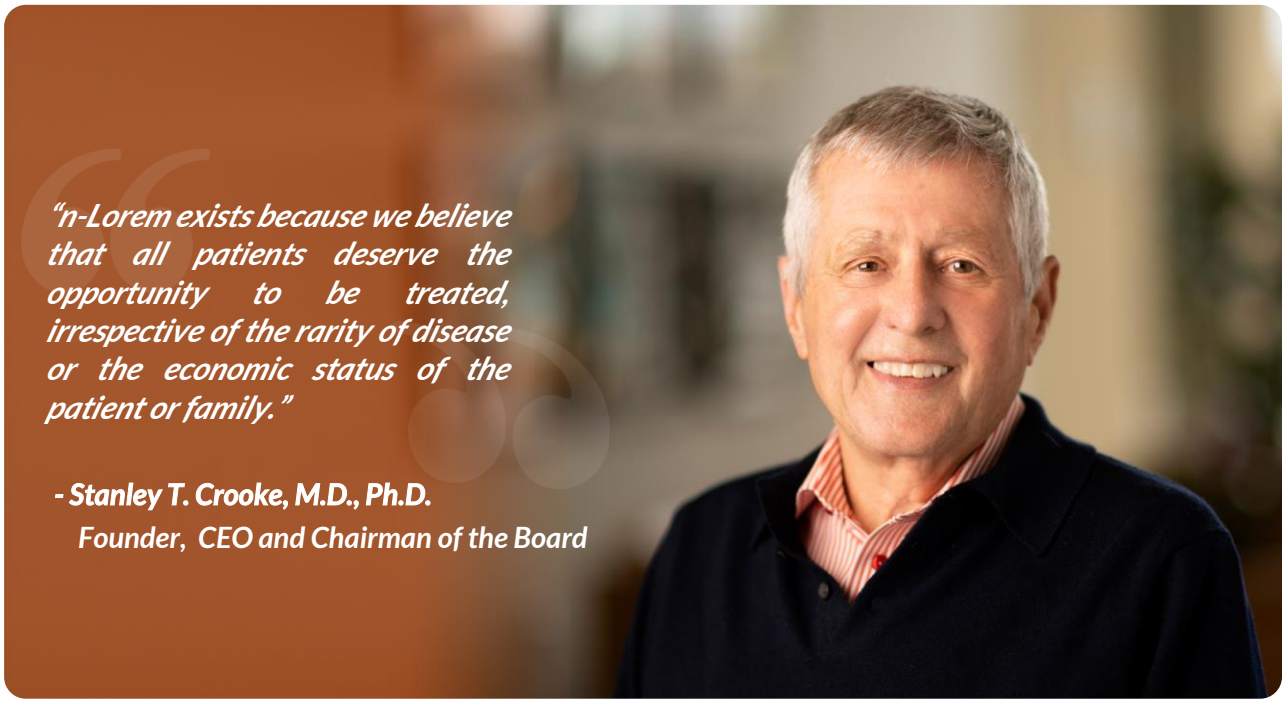
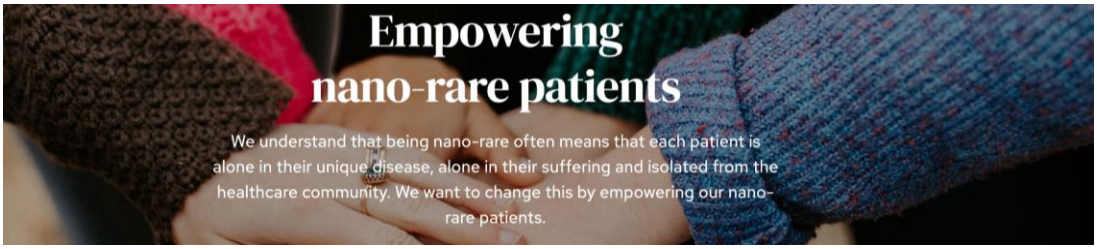


Dear supporters, partners, patients and parents,

As we enter 2023, all of us at n-Lorem know that this next year will be demanding and intense as we attempt to respond to the overwhelming demand and raise sufficient funds to support the added growth in the organization that must be achieved if we are to respond to the needs of our patients. While being intensely busy simply trying to advance ASOs for as many patients as we can afford, a major effort is underway to streamline our processes, thereby saving dollars and time and seeking solutions that will enhance the number of patients we can treat this year and beyond.

I am also quite excited that the n-Lorem team is writing several highly informative manuscripts that reflect the tip of the iceberg of what we have learned to date. As publication of scientific data in quality peer-reviewed journals is a slow process, we also plan to share key learnings through our podcast series. Importantly, the entire library of podcasts and supplemental materials for listeners is located in a new, far more informative and useful n-Lorem website.

In this annual letter, I discuss the progress we have made, but also revisit some of the most basic concepts that underlie all that we do at n-Lorem. Finally, I will provide a high-level summary of our plans for 2023.



Every Patient Matters

A core belief at n-Lorem is that every patient matters. The first dictum of therapeutics is to treat the patients who can be treated today while investing long term to identify better solutions for more patients. We know that n-Lorem cannot address the needs of all patients, but that can never justify failing to provide treatments to those who we can help today. We are committed to enhancing health care and changing the world one patient, one family at a time.

I am confident that all human beings share the view that if we can help a patient today, we have a moral imperative to do so. However, when there is a beloved family member who is suffering, it is difficult to watch other patients be treated while a loved one is not a candidate for treatment. That is an understandable emotion, but I am sure that as caring people contend with these justified emotions, they will find a way to be happy for those who may benefit from treatment while supporting those seeking new therapeutic approaches that, in the long run, may benefit ever more patients.

Promises

Every new patient represents a novel ASO discovery and development program. The essence of science is uncertainty and the process of discovering a novel medicine is complex and arduous, even for ASOs. Given this ambiguity, we can make only two promises:

- We will work as hard as possible to provide an optimal experimental ASO.
- We will assure that the clinical exposure of each patient to an experimental medicine is managed professionally by scientists with drug discovery and development experience. Every patient deserves a quality ASO that maximizes the opportunity for benefit while minimizing the risk of side effects.

Blazing New Ground

What n-Lorem is doing has never even been considered possible until the technology that was developed by Ionis Pharmaceuticals under my leadership was invented, advanced and validated. A non-profit model is the only solution available today for the rarest and most unserved population, nano-rare patients. n-Lorem is pioneering the industrialization of the discovery, development , manufacturing and provision of personalized experimental ASOs for free for life. We define nano-rare patients as those individuals who have a single gene mutation that is expressed in no more than 30 patients worldwide. Why 30 patients or less? Because there is no commercial path for such a small group of patients, and we believe that we can raise sufficient funds to provide an experimental ASO for free for life to this rarest and neediest patient population.

Though we are encouraged by the support we have received to date, the demand has outstripped all expectations and the funds we have been able to raise. Our immediate challenge is to raise sufficient funds to expand to begin to meet today's demand, then show that our model is sustainable. These are formidable challenges, but we know that n-Lorem is the best hope for these unserved patients.

Today we have received well over 160 applications and approved more than 80 patients for treatment

> 80 Patients approved for treatment

Response To Demand

As I have discussed in previous communications, the demand for experimental ASO treatment has exceeded all of our expectations. In fact, at the close of 2022, we had received more than 180 applications for treatment and had accepted more than 80 patient programs for treatment. We anticipate the demand to continue to grow significantly in 2023. In response, we have expanded far more rapidly than planned. The senior leadership and next level leadership teams are now fully staffed. Every individual we have added is experienced and has a track record of success in their area of expertise and all are cohesive and highly effective, despite the newness of the teams.

We have opened a new facility that includes a well-equipped laboratory that more than triples our capacity to discover and develop experimental ASO treatments for nano-rare patients. We expect to expand our basic research and ASO discovery and development activities significantly beyond where we are today as we get our new lab up and running. In 2023, I plan to lead basic research and advance the technology with the goal to tackle some of the more challenging ASO patient programs and enhance the performance of our ASOs.

One of my major concerns as I founded n-Lorem was that it might be difficult to recruit truly talented experienced scientists, physicians and other key members of our team since, as a non-profit, we cannot match the salaries of for-profit companies. Nor can we provide the stock options or restricted stock units (RSUs) that corporations offer. I am gratified that the reason so many talented people have joined us is the mission.

4 INDs Filed in 2022

10 INDs to be Filed in 2023

Importantly, in about two weeks in August of 2022, we filed four Investigational New Drug (IND) applications. INDs are the regulatory documents required before treatment of a patient can begin, and these INDs were submitted to two different divisions of the FDA and were rapidly approved. As a result, we are now treating patients and will be filing many more INDs this year. In fact, our minimum goal is to file at least 10 new INDs, but if we can continue to generate sufficient financial support, we have the capacity to double this number in 2023.

Communication

Since inception, we have published a number of peer reviewed manuscripts, given hundreds of presentations in which we described our mission, our quality processes and described each step in the screening process we use to identify the optimal ASO for each patient and issued scores of press releases. Though we cannot guarantee that there will be no side effects, we are committed to exposing the very sick patients who we treat to only the most prudent of risks. Importantly, as we learn more, we continue to refine our screening process to shorten the time and reduce cost while assuring the most optimal ASO possible.

Our podcast series has been very well received and, new this year, we will leverage this communication tool to reiterate our drug discovery and development process in detail. Although we have communicated this process before, we think that it is so important for all interested individuals to understand the quality processes we have created, why each step in the creation and evaluation of an experimental ASO is critical, what is learned in the identification of an optimal ASO and why it is so important. As such, we will augment our current interview and science lectures with a podcast series where we will discuss in detail each step in the n-Lorem process. We will describe how each activity contributes to the time and cost of developing an optimal ASO and how important quality and ensuring only the most optimized ASOs are developed. All ASO programs present unique challenges and in this series, I also will highlight several programs that have presented significant time delays as illustrations of what can introduce extended timelines into our programs.

More than 20 episodes

Patient Empowerment Program Podcast Series

Empowering Patients

I am also proud our progress in empowering and educating our patients, parents and other interested parties. Our podcast series consists of a mix of interviews and science "lectures" that provide a basic understanding of health, disease and treatments beginning with what a chemical is. The audience for our podcast series continues to grow and we have many exciting and informative podcasts that will be coming your way in 2023. In fact, we are adding two new podcast formats, the podcast I discussed above and a quarterly Q&A podcast.

Social Media

Additionally, we have strengthened our presence on social media. Recently, for example, on my LinkedIn page, in the "Let's discuss science" series, I provide a guide as to how to think about possibly drug side-effects, "How to think about drug related toxicities", that you might find of value. Lastly, we have been working for some time to create a much more informative and accessible website that we launched earlier this month.

Another important type of communication concerns the status of specific ASO programs for specific patients. Not surprisingly, we are asked by patients and parents frequently about the potential for success in identifying an ASO and the progress and timing of when an ASO will be available to treat that patient. As a general rule, we think that such communications should be between the treating physician and the patient or parent. When appropriate, we provide information to be discussed directly to the treating physician, who will continue to communicate with the patient or parents.

We will continue to try to optimize our approaches to communication and look forward to your comments and suggestions.

Health Equity

n-Lorem exists because we believe that all patients deserve the opportunity to be treated, irrespective of the rarity of the disease or the economic status of the patient or family. If we can prolong and enhance the life of a patient and return hopes a dreams to a family, we are morally obligated to do it. We focus on patients who have diseases caused by a single gene mutation that is found in no more than 30 patients in the world. We choose this patient population because today there is no path to commercial approval or commercial model that can address the needs of such rare patients and because we hope that we can raise sufficient donations to treat as many nano-rare patients as we are able to.

We are industrializing the treatment of nano-rare patients because we believe that each patient deserves the very best ASO that we can discover and develop and the professional management of the exposure of the patient to an experimental medicine. We have established quality processes that assure that each patient is treated with an optimal ASO. Our process begins when an application for treatment is received. The application is blinded, meaning that we have redacted all personal details on the patient. When evaluating an application, the only factors considered are the prevalence of the mutation, the feasibility of treating the patient with ASO technology, the status of the patient, the rate of disease progression and the availability of a research physician committed to treating the patient and evaluating the performance of ASO at an institution capable of and committed to the treatment of a patient with an experimental medicine. The economic status of the patient is not considered. Nor is the question of whether the patient or family is a donor considered. Unless a patient or parent contacts n-Lorem or discloses the identity of the patient publicly, we are blinded to the identity of each patient.

Treating Patients With the Rarest of Mutations Is A Moral Imperative And Treatment of One Will Benefit All Patients

Though many of our patients have mutations that cause illnesses that have never been identified or named, we now know that for almost all rare genetic diseases, there are typically one or two mutations that account for most of the afflicted patients and multiple extremely rare mutations that may cause disease in one to a few patients. On occasion, for patients with a known and named disease and a patient advocacy group, we are asked how the treatment of one or a few patients with the rarest of the mutations that cause the disease helps those who are not candidates for n-Lorem provided experimental ASOs. Our answers to these questions are described below.

1. Why Treating One Patient Benefits All Patients With A Rare Disease

As I discussed above, the most compelling reason to treat a patient is that every patient matters. As we age, we learn that what were black and white tenets are many shades of gray. Not so for the belief that every patient matters. I say this with absolute moral certitude that has informed my life and career and is why n-Lorem exists. That said, though there are other compelling reasons to treat even one patient in a population of patients with the same disease, but perhaps not the same mutation.

2. All Knowledge Matters

Advances in science are incremental and each additional bit of knowledge contributes to the evolution of understanding. No area of scientific inquiry is more incremental than advances in the treatment of diseases. What can be learned by addressing the needs of patients with the rarest of mutations that cause a more common rare genetic disease is immediately applicable to the entire group of patients with the disease. There is no better way to learn about the molecular causes of a disease and potential value of therapeutic interventions than studying a patient or a few patients, even if they have the rarest of the mutations known to cause the disease.

3. Acquiring A Corporate Partner To Commercialize A Medicine For The Entire Disease Population

When a biotechnology or pharmaceutical company must make a development decision, even for a rare disease drug, the investment is likely a minimum of $100 million. The key problem at the time such decisions must be made is that the intrinsic failure rate of drugs at that stage demands that any future value must be discounted by 80-90% and then the economics simply do not work for any reasonably sized company. The hard truth is that there are simply better ways to invest shareholder money. This means that products for small patient populations are usually not developed commercially and today, this basic math is exacerbated by the fact that current pricing of rare diseases drugs is under pressure. Unfortunately, the best way to reduce risk meaningfully is to obtain positive clinical data in a few patients with a disease. n-Lorem is uniquely positioned to treat patients with the rarest of mutations known to cause the disease and determine if the experimental ASO appears to be beneficial.

Further, the leadership of n-Lorem has decades of experience in partnering in the drug discovery industry and is committed to using the data to find a responsible commercial company to develop a medicine for the disease in question. In fact, there is already an example of the success of a personalized ASO encouraging full commercial development for a rare disease.

4. Industrialization of the Treatment of Nano-rare Patients

I have emphasized how vitally important it is to work with scientists and physicians thoroughly knowledgeable and experienced with ASO technology to assure that patients are exposed to only optimal ASOs. Additionally, I have also spoken and written repeatedly about how vital it is to assure that the clinical exposure of patients to experimental medicines of any type be managed by those experienced in managing the development of experimental medicines. To my mind, these concepts are so self-evident as to be unworthy of discussion. Just as it would be foolish and dangerous for me, even though I am an M.D., Ph.D. with house staff training in internal medicine, to take care of a child with a complex neurological disease, it would seem equally foolish and dangerous for a physician who has never contributed to the basic advancement of antisense technology or developed a new drug, to try to discover and administer an optimal ASO. In short, I have warned of the dangers posed by "amateur ASO makers" repeatedly and offered to collaborate with any competent clinician. Gratifyingly, almost all academic physicians have chosen to work with n-Lorem.

Conclusions

n-Lorem is off to a strong start, but we are not even at the end of the beginning of the journey to bring hope and help to patients with nano-rare mutations. I am pleased that the quality systems we developed are working, I am thrilled to be treating multiple patients with many more INDs coming and I am proud of how hard we have worked to communicate about what we are doing. However, we know we can to more and do it better. We are looking forward to the even more effective approaches to communication approaches that I mentioned and to enhancing many elements of the processes we have created.

In the next installment of my annual letter, I will focus on our plans for 2023 and beyond and the exciting things we are learning. I look forward to serving many more nano-rare patients and sharing all that we learn with you.

Stanley T. Crooke, M.D., Ph.D.