



Dear Friends and Colleagues,

As we conclude 2023, though I know that we have many challenges ahead of us, I am ever more confident in the value of our mission and the future of n-Lorem. The confidence in our future is a product of the outstanding progress we have made this year, building on the momentum of our first three years, and I am pleased to share a few highlights with you in this letter while I extend best wishes for a joyous holiday season and wonderful 2024.

Delivering on our promises

We have now filed 10 INDs in four divisions of the FDA. We have treated six patients and hope to initiate treatments in the other patients shortly. As you know, even after the FDA has performed a thorough review of an IND, each institution in which a patient is to be treated reviews the treatment plan, the information that assures that treatment with the ASO designed for that patient is appropriate, and that review by the treating institution can take a number of weeks. Even more encouraging is the clinical experience as a number of our patients appear to be experiencing meaningful benefit from their ASO and the safety and tolerability are pristine, despite how progressed in their disease our patients are.

Equally important, we have completed the building, equipping and staffing of our main laboratory, which is now fully functional and delivering great results. This means that we can begin to make real progress in working through the many cases we have accepted for treatment and to initiate research activities that will improve the performance of our ASOs

and hopefully increase the types of patients we can treat. To substantially improve the efficiency of our lab and accommodate growth, almost immediately after we completed the build-out of our lab, we are moving to a new, better, more efficient, larger lab, which, as a bonus, will allow us to consolidate all our San Diego team at a single site.

Sharing what we know and what we are learning

Knowledge and experience with ASO technology are critical requirements to provide effective and safe ASOs to nano-rare patients. Also important is real experience in drug discovery and development and it is vital to manage patients exposed to experimental medicines professionally. The n-Lorem team brings decades of ASO experience and a deep understanding of drug discovery and development to bear on the opportunities and challenges we encounter. It is important that we share what we know, how we identify optimized ASOs, our experience in the clinic and all that we are learning from nano-rare patients with all interested parties.

Because I believe that science is never done till shared with peers in a high-quality peer-reviewed journal, we emphasize scientific publications as a key venue in which we can share. We have now published eight peer-reviewed manuscripts, with clinical investigators have submitted case reports of nano-rare patients who have been treated and written a major paper describing the characteristics of the first 173 patients who applied for treatment. As that manuscript is in revision in a major scientific journal, I am optimistic that it will be published next year.

On the other hand, it is important that we share all that we know and are learning in a more timely fashion than peer-reviewed manuscripts. To that end, we have made hundreds of presentations. Most importantly, in 2023, we held our first nano-rare patient colloquium, which was generously hosted by one of our founding donors, Biogen. By all measures, that meeting was a great success. We presented what we do, how we do it, and what we are learning in detail and listened carefully to our patients and families and partners. Attendance was excellent and we are looking forward to our 2024 colloquium.

Working effectively with regulators

Throughout my career I have believed that if we put the needs of patients at the center and never waver from our commitment to do what is best for the patient, then couple that to a deep understanding and respect for the challenges of drug development, high quality science and transparency, regulatory interactions will be constructive. At Ionis, I led the creation of this technology and the establishment of a rigorous, transparent scientific environment. I believe that one of the reasons that the special guidance for ASOs for nano-rare patients exist is the reputation we established at Ionis. At n-Lorem, we have maintained that commitment and refined it as we think about the needs of individual patients. We continue to work effectively with the FDA because we share a commitment with them to help nano-rare

patients while exposing our patients to only prudent risks. We will continue to do all that we can to earn the FDA's respect and trust every day as we enter 2024 and beyond.

Creating the highest quality, most committed team possible

Our patients deserve the efforts of the highest quality team and it has been my goal to achieve that. But I worried that we might not be able to recruit outstanding leaders because we cannot offer the financial rewards of commercial companies. I am pleased to tell you that I needn't to have been worried. The mission is the only recruiting tool I have needed and, in 2023, we completed building the senior leadership team, the mid-manager team and the laboratory team and every position is held by an outstanding person. I am confident when I say that I have never had a better, more committed, more cohesive team than I have at n-Lorem. We focus our outstanding team on meeting the unique needs of each of our patients and the quality of the team is displayed in every ASO for every patient.

Taking center stage

n-Lorem is unique in vision, scale and quality. Thus, a major goal in 2023 was to assure that n-Lorem and our unique qualities were broadly known and understood. We think we achieved that in 2023. The growth in the popularity of our podcast series, the success of our nano-rare colloquium, our national media coverage and our social media presence are evidence of that success.

Fundraising

2023 was another successful year in fundraising. We exceeded our challenging fundraising goals again this year and opened multiple new funding sources as well as continuing support from past donors. We enter 2024 with numerous opportunities we are pursuing. Of course, the more we succeed, the more funding we need, but I do see a path to sustainable financing, and we are ahead of schedule in achieving that goal. Once again, the primary reason I can say that is the rightness and power of our mission. That said, we will need your help and every dollar matters.

2024 and beyond

We enter 2024 with great momentum and optimism. We will be able to do more and do it better. Please join us as we do our best to change the world for the better, one patient, one family at a time.



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