



June 30, 2022

DEAR COLLEAGUES, PARTNERS, AND SUPPORTERS,

I am pleased to have the opportunity to provide an update on the progress that we are making at n-Lorem. I hope that you agree that what we have accomplished to date is impressive, but more importantly sets the stage for bringing ever greater value to our patients.

PATIENT TREATMENT AND DEMAND

As our mission is entirely focused on helping nano-rare patients, the single most important area of progress will always be patient-centered. I am pleased to tell you that Dr. Neil Shneider continues to report that the FUS ALS patients being treated with an experimental ASO continue to gain strength and improved function.

The next step is, for us at n-Lorem, very exciting. We expect to initiate treatment of five to eight new patients before the end of 2022. Demand continues to be high. We have now received over 150 applications and have accepted 69 patients for treatment. One informative way to think of n-Lorem is that we are two-and-a-half-year-old biotechnology drug discovery effort with more than 60 drug discovery programs, more than 20 drugs in development, five to eight of which will begin clinical administration this year. Even though what we do at n-Lorem is very similar to what is done routinely in drug discovery and development at Ionis, each step in the process is sufficiently different that we have had to create entirely new systems and processes.

Given all that, I think you can readily understand that our tiny core team has been stretched to our limits, but we are achieving great things and enjoying every moment of it.



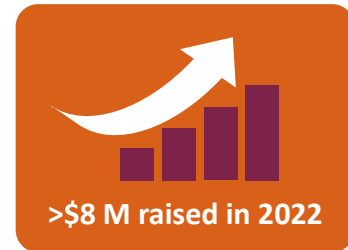
“What we have accomplished to date is impressive, but more importantly sets the stage for bringing ever greater value to our patients.” Stan Crooke, M.D., Ph.D., CEO and Founder of n-Lorem Foundation



FUNDRAISING

Despite the successes we had in fundraising in 2020 and 2021, as we entered 2022, I felt that achieving our goal of raising \$8M was going to be extremely challenging. Nevertheless, by the end of this month, we will have raised approximately \$16M and given the numerous opportunities and leads that we have developed, I am optimistic that in the remaining months we will continue to be very successful in fundraising. The central reason for our success is our compelling mission.

I am confident that we will enter 2023 with great momentum and an expanding base of donors, partners and supporters. To all those who have contributed, on behalf of the patients we serve, you have my deepest appreciation.



ORGANIZATIONAL DEVELOPMENT

Because of our success in fundraising, we have greatly accelerated our growth. We have established a senior leadership team that is truly outstanding, cohesive, committed and intensely demanding of ourselves and others. In recognition of her outstanding performance, the Board of Directors and I recently promoted Sarah Glass, Ph.D., to Chief Operating Officer. We are now filling in the next level in the leadership and management team and well along in completing the recruitment of a second laboratory. The second laboratory will be fully up and running by the end of this year and will double our capacity to advance the cases that we have accepted for treatment. I fully expect to be able to respond to each patient more rapidly and more effectively. Perhaps of even greater long-term importance, with the new lab and staff we are beginning to invest in core research that will address issues like being more efficient in discovering allele-specific ASOs.

Despite the demands for high-quality scientific and medical talent, we are thrilled with the quality of individuals who have chosen to join us. Once again, I am confident that our success here is driven by our mission.

FDA INTERACTIONS

Though we were very pleased that the FDA responded rapidly to provide detailed guidance specific for ASO experimental therapy for nano-rare patients that included many of our suggestions, we could not know how effective our interactions with individual divisions would be. Once again, at the risk of sounding like a broken record, the interactions with the divisions to date have been very supportive and the public posture of the FDA continues to be supportive.



COMMUNICATIONS/PARTNER AND DONOR RELATIONS

Since Amy Williford joined us the progress here has been wonderful. Our new presentation has been extremely well received, we have issued many positive press releases with more to come, our speaking engagements reflect the interest in having the n-Lorem model included in important discussions, and our contributions evidenced in the publication of important peer reviewed articles. Shortly, we will unveil a new website that will include better support to help patients find an appropriate center for diagnosis and treatment and support for institutions.

QUALITY SYSTEMS

It is vital that every step in the process be of the highest quality possible if we are to maximize the opportunity for benefit and minimize the risk of adverse events in our patients. We now have enough experience with our quality systems to be confident that they are working and that only appropriate patients are treated with the very best possible ASOs. We hope that some of organizations less experienced in ASO discovery and development adopt some of our quality systems.

LEARNING FROM OUR PATIENTS

I have adopted an expression first used by Thomas Jefferson to describe the Lewis and Clark Expedition. Jefferson referred to the expedition as the *Corps of Discovery*. To my mind n-Lorem in its own way is a corps of discovery for both the mind and the heart. Certainly, for me every day is an opportunity to learn intellectually and emotionally from our patients. To that end the approaches that we have developed to collect natural history data and to compare those data to results during treatment are critical to maximizing what we learn. We believe that our systems that are in place and are ready to maximize learning from each patient as we expand from five to eight patients this year, to many more next year and thousands in the decades to come, but as we gain experience, I am sure that we will continue to learn and refine our systems. In this effort, we are greatly aided by our partner, Parexel.



Today we have received well over 150 applications and approved more than 60 patients for treatment



> 60 Patients approved for treatment

PARTNERSHIPS

We continue to benefit from many partnerships we have already established with vendors that provide services to our industry, including manufacturing, sterile fill, GLP toxicology studies and clinical trial services. In our latest presentation, you will find a slide that lists our partners, each of whom is making significant contributions to our ability to treat more patients with higher quality. We have been quite successful this year in adding new partners and donors, and we are just getting underway. By the end of 2022, I expect that our roster of partners will be too large to show on a single slide. The response has been overwhelmingly supportive. Once again, the reason for the support is the mission. Everyone recognizes the gravity of the challenges that nano-rare patients face and the need for all of us to come together to create a community that can bring hope, help and benefit to these patients.

PATIENT EMPOWERMENT PROGRAM

We are very pleased to have launched this program with our podcast series. The goals of the podcast series are to provide a forum where the voices of patients, advocates and experts can come together focused on the nano-rare patient, and to help nano-rare patients and family to better understand why their lives are affected by these mutations and how challenging it is to address some of the problems via a series of didactic chats that go from the most basic to the complex task of understanding disease and creating treatments for the disease.



Available NOW!

Patient Empowerment Program
Podcast Series



CONCLUSION

In this brief communication, I have shared a tiny bit of the progress that we are making. We are proud of the progress, but we understand that we have just started and the challenges that lie ahead must be met, and we must prove that a non-profit model is sustainable. We are buoyed by the progress that we have made and never more confident that with your help we can meet the challenges and prove that human hearts are big enough to address the needs of the nano-rare patient with a sustainable non-profit model.

A handwritten signature in black ink, appearing to read "Stanley T. Crooke".

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