**Script - What is n-Lorem?**

Hello. Welcome to the n-lorem podcast series that focuses exclusively on patients that we now refer to as having nano-rare mutations. I’m Stan Crooke, and I’m the founder, chairman and CEO of n-Lorem.

n-Lorem is a charitable foundation I founded in January 2020. Our mission at n-Lorem is to take advantage of the technology we created at Ionis Pharma, antisense technology, to discover, develop, and provide experimental antisense (or ASO) treatments to nano-rare patients for free, for life.

So, let’s begin with defining what a nano-rare patient is. A nano-rare patient is a patient with a disease caused by a mutation that is oftentimes unique to that patient and that patient only. In some cases that mutation may cause disease in up to only 30 patients worldwide.

The rarity of the mutation, and therefore the disease, is the core problem. Most patients with nano-rare diseases are never diagnosed; and the fortunate few who are diagnosed typically spend years being referred from one specialist to the next before being referred to a tertiary care center, where they can be genetically diagnosed and fully characterized clinically.

This group of patients is the most isolated, underserved, and desperate population that I have encountered. The limited number of patients means that the commercial development of a drug for these patients is essentially impossible. That is where n-Lorem comes in.

Though n-lorem is only two years old, more than five years ago I realized that antisense technology, or ASO technology, could in principle, help many of these patients. Several other elements needed to be in place before n-Lorem could be feasible. The first step in the process of treatment is, of course, diagnosis. Diagnosis for a patient with a nano-rare mutation requires genomic sequencing, characterizing the function of the gene in question, and understanding the manifestations of the disease in the patient.

Such activities can only be achieved in the most sophisticated of settings, tertiary care, research-focused, medical centers. Fortunately, over the last decade or so, a consortium of tertiary care centers, called the Undiagnosed Diseases Network, or UDN, has made great progress in accessing undiagnosed patients and making diagnoses as well as doing all the necessary work that I described above. So, among the first collaborations at n-Lorem was the collaboration with the UDN. The UDN has contributed quite a number of patients to n-Lorem, but there are now a few other personalized medicine centers. So now many of our patients are coming from other personalized medical centers.

The next critical element was to ensure that there was a supportive regulatory environment. Because the discovery and development of treatments for patients in urgent need must be very rapid and cost-effective, special guidance is required from the FDA and other regulatory agencies to ensure that providing experimental treatment is possible. Fortunately, the FDA has been highly responsive and has issued guidance specific to the provision of experimental ASO treatments at no cost to nano-rare patients. Today, the only technology for which special guidance has been issued is the technology that we bring to bear to help these patients, ASO technology.

The founding donors of n-Lorem were the company I created and led for 30 years, Ionis Pharmaceuticals, our partner in the neurosciences, Biogen, and my wife and I. Since our foundation, we have added numerous partners and donors, and that has supported rapid expansion to meet the demands we have experienced.

The name n-Lorem first derives from an abbreviation for a number, n, and the concept of therapy. So, n-Lorem signifies bringing treatment to patients who are unique, who are members of a true nano-rare patient population.

And indeed, the demand has been extraordinary. When I began n-Lorem I thought that perhaps by now we might have a handful of applications for treatment and that we would be able to manage n-Lorem essentially with all volunteers for the first two years. In fact, while we were setting up n-Lorem, we had the opportunity to help 14 patients to be treated with personalized experimental ASO therapies, and we now have well over 130 new applications and are proceeding toward treating more than 50 nano-rare patients. As we look out over the longer term, it is clear that we will be treating thousands of patients. So, the technology must be scalable and fortunately, it is. We have expanded very rapidly to try to meet this extraordinary demand, but we are still playing catch up. We are optimistic that we will meet our goal of treating patients within 12 – 18 months of receiving the application.

To put that in context for you, the discovery process for a drug to a novel target is 10 – 12 years and hundreds of scientists, and the development takes on average 16 years. We have to do this because by the time patients are diagnosed, genetically characterized, and referred to us, they are in desperate need of treatment and every day matters.

From inception, we have known that we cannot do this alone. So, we have been very successful at putting together a growing network of stakeholders, donors, partners and clinical research sites that we call partners in excellence. These partnerships have allowed us to reduce cost per patient by more than 40% from the remarkably low cost that we began with.

But we have just begun, and we have an important and exciting and challenging set of tasks before us. One of the most important contributions we hope to make is to create a community for these very isolated patients and provide solid knowledge and experience to help patients understand the process for their treatment and a sense of community. This podcast series is a part of a program that we call the patient empowerment program. In coming episodes, we look forward to providing more interviews as well as a series of more didactic episodes that focuses on bringing power to patients through knowledge.