

The n-Lorem Foundation Mission

The mission of the n-Lorem Foundation is to apply the efficiency, versatility and specificity of antisense technology to charitably provide experimental antisense oligonucleotides (ASO) medicines to treat patients with ultra-rare diseases (<10 patients).

Challenges of Treating Patients with Ultra-rare Diseases

Patients with ultra-rare diseases (n1-10) present compelling unmet needs. Challenges to treating these patients include:

- **Diagnosis:** most often, genetic screening is needed to diagnose patients with ultra-rare diseases
- **Genetic characterization:** once diagnosed, patients need to know if their disease is caused by a genetic mutation, and if so, what that mutation is
- **Physician specialist:** patients need a physician experienced with treating their disease
- **Medical institution/facility:** patients should be treated at a medical institution or facility that is properly experienced and equipped to treat patients with their disease
- **Individualized treatment:** patients need a medicine that is designed specifically to treat the genetic cause of their disease
- **Regulatory approval:** individualized treatment will usually require regulatory approval

Traditional biotech and pharmaceutical companies are ill-equipped to address these needs because the drug platform technologies they employ, such as small molecules, therapeutic proteins or antibody drugs, are not well-suited for creating individualized medicines. Costs and resources needed to develop new individualized medicines for ultra-rare disease patients with a broad diversity of diseases are prohibitive.

An Answer to the Challenges of Treating Patients with Ultra-rare Diseases: While no single charitable institution can meet the needs of these patients, n-Lorem, in conjunction with Ionis Pharmaceuticals, other organizations that are dedicated to patients with many of the ultra-rare diseases, such as the Undiagnosed Diseases Network (UDN) and working in compliance with regulators, can bring hope and benefit to the underserved.



Creating Individualized Treatments for Patients with Ultra-rare Diseases Using Antisense Technology

Advances in molecular biology now allow for relatively inexpensive DNA sequencing that supports the identification of the genetic causes of many diseases.

- Some ultra-rare diseases are caused by a single genetic defect unique to only one or very few individuals.
- ASO's are short strands of modified DNA that can specifically target the transcripts of a defective gene to correct the abnormality. The advantage of experimental ASO medicine is that they can be developed rapidly, inexpensively, and are highly specific.

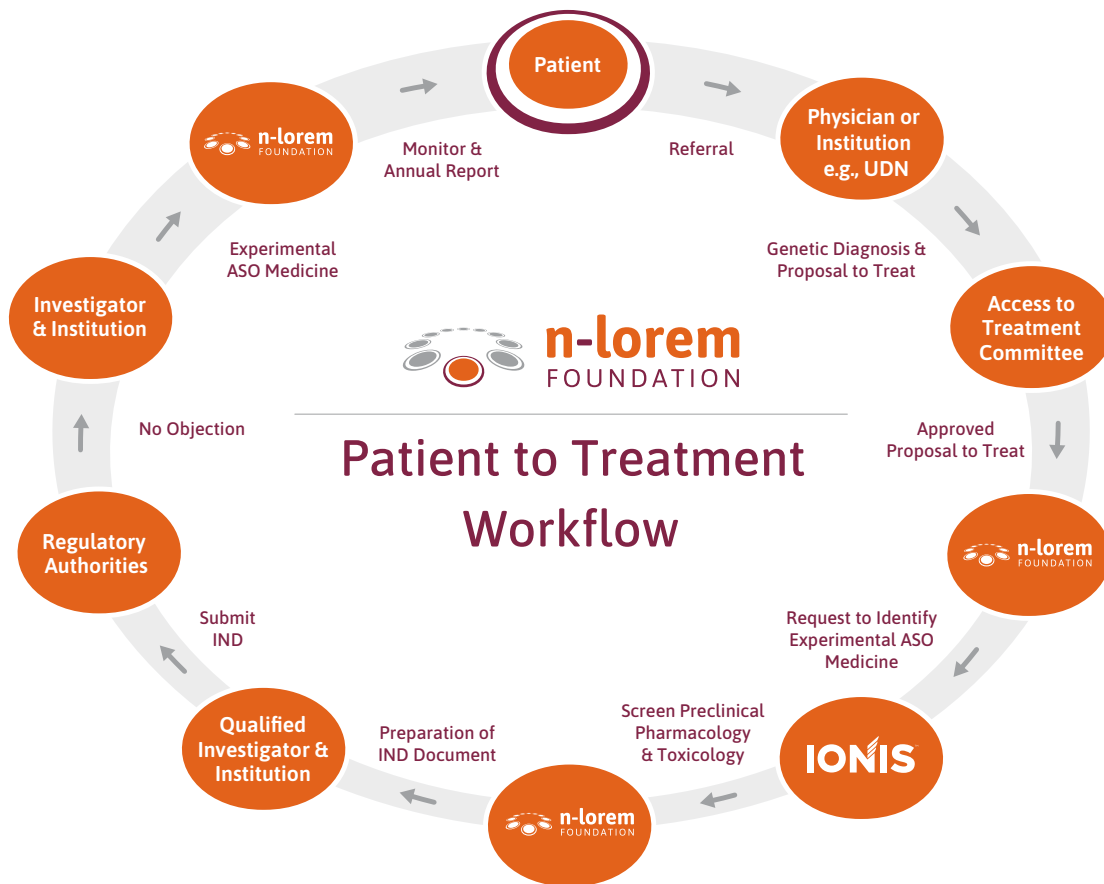
n-Lorem works as a public-private partnership together with Ionis Pharmaceuticals, the leader in RNA-targeted therapeutics, to develop custom experimental ASO medicines for patients with ultra-rare genetic diseases.

How the Foundation Works

With a seasoned leadership team and strategic partnerships, the n-Lorem Foundation provides the framework and funds for the treatment of appropriate patients with experimental antisense oligonucleotide (ASO) medicines. See “Workflow from Patient to Treatment” and “Access to Treatment” for further details.

The Foundation’s Access to Treatment Committee (ATC) [see “Access to Treatment” for more details] will review patient referrals from physicians, medical institutions and organizations that are dedicated to patients with ultra-rare diseases, such as the Undiagnosed Diseases Network (UDN). These individuals and organizations will be instrumental in identifying and evaluating patients with genetic anomalies who could be treated with an experimental ASO medicine. Once diagnosed patients with a genetically defined ultra-rare disease are approved for treatment with an experimental ASO medicine by the ATC, Ionis Pharmaceuticals, the leading innovator in RNA-targeted therapeutics, can:

- Develop a personalized precision experimental ASO medicine for each patient selected into the program.
- Perform *in vitro* and *in vivo* studies to evaluate the efficacy and safety of experimental ASO medicine candidates and choose the best experimental ASO medicine for treatment.
- Work with clinical investigators to generate and submit an Investigational New Drug (IND) application to the Institutional Review Board and the Regulatory authorities.



Upon regulatory permission of the experimental ASO medicine, an investigator-led clinical trial can then be initiated, in which individual patients will receive their experimental ASO medicine. The Foundation plans to provide the experimental ASO medicine free of charge to patients for the rest of their lives.



Individualized Treatments for Individual Patients

We can do this! The technology is already here. n-Lorem and its partners are ready to evaluate patients with rare genetic diseases who may benefit from treatment with custom experimental antisense oligonucleotide (ASO) medicines.

Child with fatal brain disease treated with experimental ASO medicine

A child who experienced progressive loss of vision, epilepsy and neurological deterioration was found to have a unique mutation in a gene caused a variation of Batten disease. The child has been treated with an experimental ASO medicine and the child's disease may be progressing less rapidly.

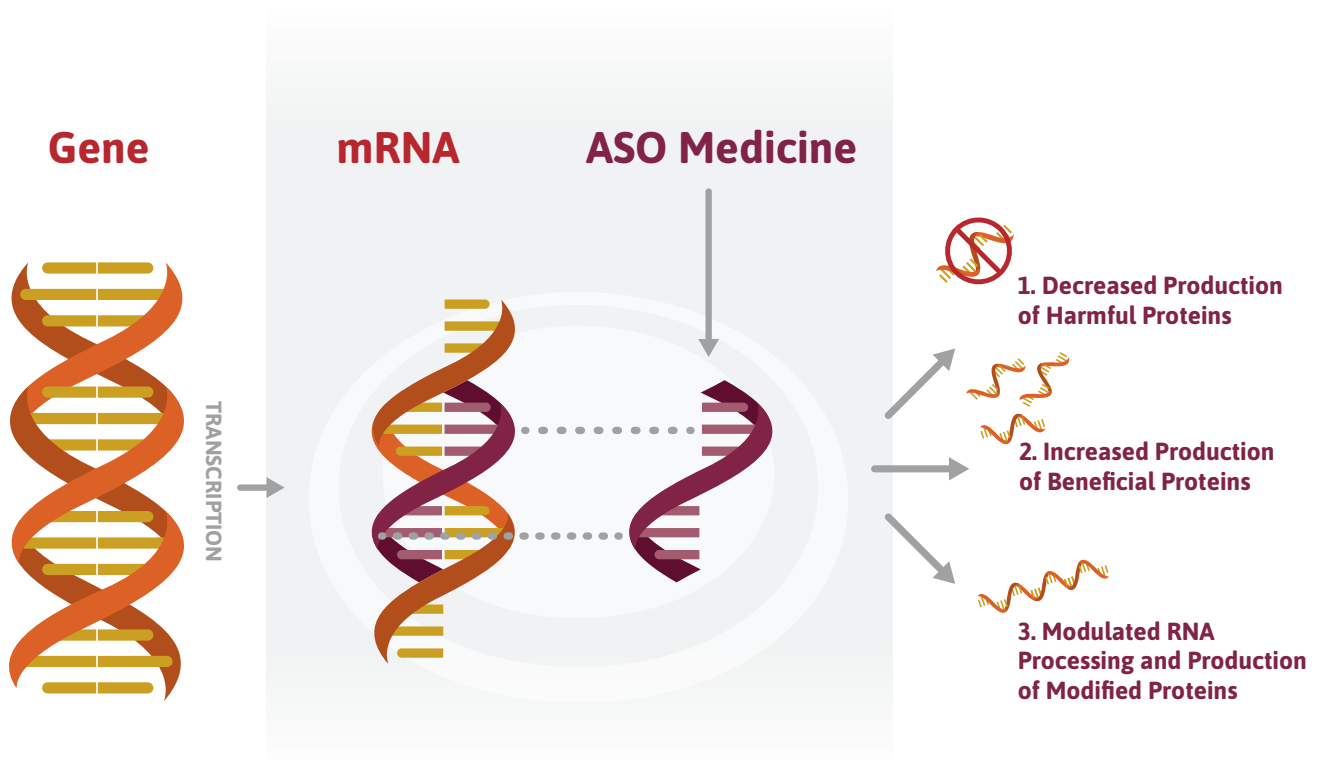


A child with progressive loss of vision and the ability to walk treated with an experimental ASO medicine

A child born with an inability to feel pain experienced progressive deterioration in vision and was found to have a unique mutation that is causing posterior column ataxia and retinitis pigmentosa (PCARP) is receiving an experimental ASO medicine to try to prevent further vision loss and preserve the young patient's ability to walk.



ASO Medicines Target the Messenger, Not the Protein Product



Access to Treatment

How do patients get access to treatment?



For Patients and Their Caregivers

Step 1: Seek a diagnosis

The first step toward potential treatment is to achieve a diagnosis and full genetic analysis. If the caregiver or institution is unable to achieve a diagnosis and perform a full genetic analysis, patients or their caregivers should contact physicians and institutions capable of achieving these essential goals. n-Lorem recommends contacting the Undiagnosed Disease Network (UDN) at <https://undiagnosed.hms.harvard.edu/> or 1-844-RING-UDN (1-844-746-4836) or similar organization. The UDN is a consortium of physicians and institutions focused on using modern genetic methods to characterize difficult to diagnose patients.

Step 2: Submit a proposal for treatment

Once a diagnosis and full genetic evaluation is completed, two paths toward evaluation of the appropriateness of experimental antisense oligonucleotide (ASO) medicine are available. To submit a request for treatment directly to n-Lorem, the patient or guardian must grant permission for the caregiver to share information about the patient with n-Lorem via the online proposal submission form at nlorem.org/access. n-Lorem will then submit the request for treatment to the Access to Treatment committee for evaluation. Alternatively, the patient and care-giver can submit a request for treatment to any member, physician or institution of the UDN. The member of the UDN would then submit a request for treatment to the n-Lorem Access to Treatment committee. In either case the caregiver must complete an Access to Treatment request form that can be found at nlorem.org/access.

To make an informed decision about whether a patient is appropriate to receive treatment with an experimental ASO medicine, substantial information concerning the patient and the genetics of the patient must be provided.



Access to Treatment Committee

Our Access to Treatment Committee is made up of pharmaceutical executives, physicians, academic professors, patient advocates, and a bioethicist. This committee will review proposals from physicians or organizations, like the UDN, to treat diagnosed, genetically confirmed ultra-rare disease patients. Proposals will be approved and prioritized based on criteria such as: feasibility of developing an experimental ASO medicine for the genetic cause of the disease, degree of potential benefit of treatment, practicality of treatment, availability of physician and institution to treat patient and conduct necessary studies, and other complexities of the condition.

At the Foundation we understand that there are seriously ill patients with immediate needs of a treatment for their condition. We are sympathetic to patients, families and caregivers involved and we plan to do all we can to make sure we are as transparent as possible. Due to the complex nature of treating patients with ultra-rare diseases, the Access to Treatment Committee cannot approve all proposals for treatment, however the Committee will fully review all proposals received before a decision is made.

- **Walter Singleton, MD, Co-Chairman** – *Chief Medical Officer at n-Lorem*
- **Frank Bennett, PhD, Co-Chairman** – *Chief Technology Officer at n-Lorem and Chief Scientific Officer at Ionis Pharmaceuticals*
- **Matthew Might, PhD** – *Director at Hugh Kaul Precision Medicine Institute at University of Alabama at Birmingham*
- **Kristina Bowyer** – *Patient Advocate at Ionis Pharmaceuticals*
- **Alan Beggs, PhD** – *Professor of Pediatrics at Boston Children's Hospital*
- **Francis Sessions Cole, III, MD** – *Professor of Pediatrics at Washington University School of Medicine in St. Louis*
- **Eric Swayze, PhD** – *Vice President of Research at Ionis Pharmaceuticals*
- **Eugene Schneider, MD, PhD** – *Vice President and Head of Clinical Development at Ionis Pharmaceuticals*
- **Matt Buck, JD** – *Vice President of Regulatory Affairs at n-Lorem*
- **Alfred Sandrock, Jr, MD, PhD** – *Executive Vice President of Research & Development and Chief Medical Officer at Biogen*

Governance and Leadership of the n-Lorem Foundation

“Leadership is the Capacity to Translate Vision into Reality” - Warren Bennis

The n-Lorem Foundation recognizes that its success depends upon its leadership and strategic partnerships. The foundation's carefully curated leadership team is composed of industry veterans who have dedicated their lives to improving patient lives. Heading the foundation as CEO and Chairman of the Board is Dr. Stanley Crooke who founded Ionis Pharmaceutical in 1989 and through his vision and leadership, established the company as the leader in RNA-targeted therapeutics. With Dr. Crooke's commitment to driving the foundation forward, n-Lorem is poised to serve innumerable patients.



Board of Directors

Our board of directors is made up of pharmaceutical executives, physicians, lawyers, and academic professors. The combined experience of our board spans decades. The board will be responsible for oversight of all activities related to the foundation, including strategy, budgets, and regulatory guidance.

- **Stanley Crooke, MD, PhD** - *Founder, Chief Executive Officer and Chairman of the Board, n-Lorem*
- **Michel Vounatsos, MBA** - *Chief Executive Officer of Biogen*
- **Karen Chen, PhD** - *Chief Executive Officer of the SMA Foundation*
- **Michael Hayden, MBChB, PhD** - *Killam Professor of Medical Genetics at University of British Columbia*
- **Joseph Loscalzo, MD, PhD** - *Senior Physician & Head of the Department of Medicine at Brigham & Women's Hospital, Harvard Medical School, and Executive Committee Member of UDN*
- **Rosanne Crooke, PhD** - *Founder of n-Lorem, Senior Strategic Advisor to Ionis Pharmaceuticals*
- **Lynne Parshall, Esq** - *Senior Strategic Advisor & Former Chief Operating Officer of Ionis Pharmaceuticals*
- **Spencer Berthelsen, MD** - *Former Managing Director & Chairman of the Board of the Kelsey-Seybold Clinic*



Executive Leadership

The executive officers of n-Lorem have committed to managing the foundation's fundraising, financing, strategic communication, clinical evaluations, regulatory adherence, and its interactions with Ionis for development of custom ASO medicines.

- **Stanley Crooke, MD, PhD** - *Founder, Chief Executive Officer and Chairman of the Board, n-Lorem*
- **C. Frank Bennett, PhD** - *Chief Technical Officer*
- **Walter Singleton, MD** - *Chief Medical Officer*
- **Matt Buck, JD** - *VP Regulatory Affairs*
- **Tracy M. Johnson, MEd** - *Executive Director*
- **Kim Butler** - *Senior Administrator*