The Unparalleled Opportunity to Learn from Treating Nano-Rare Patients with Individualized ASOs

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Over three decades of experience with antisense technology enables the n-Lorem Foundation to discover, develop, and provide individualized treatments for patients with nano-rare diseases. These patients are often the only individual in the world that have their disease-causing mutation, therefore mutation-driven drug discovery and development is required. Currently, there are four FDA Guidance Documents specific to Individualized Antisense Oligonucleotides that provide a road map for drug discovery and development. When this FDA guided path is navigated with high scientific rigor, robust quality processes, and driven by the learnings from n-Lorem's three decades of experience, it can lead to an optimal ASO that may be life-saving for some individuals.

n-Lorem's rigorous process begins with an evaluation of patients for whom an application has been submitted. This evaluation is based solely on their genotype and phenotype to determine whether they believe they will have success in identifying an optimal ASO for that patient. By focusing the evaluation on only the genotype and phenotype for each patient, it ensures unbiased access to potential n-Lorem treatments for all individuals with nano-rare mutations, regardless of their economic status.

n-Lorem provides a unique opportunity to treat a patient (or handful of patients) who otherwise does not have access to treatment beyond symptom management, coupled with an opportunity to learn that is unlike any that exists today. To date, the n-Lorem foundation has accepted over 100 patients for whom individualized ASO programs are in progress; 10 INDs have been submitted; 6 patients have been treated; NO drug-related adverse events have occurred in >20 doses across all treated patients. There are multiple facets of knowledge that are already being gained from treating the nano-rare population:

1. n-Lorem has developed the only existing robust database of genotype/ phenotype data on patients with nano-rare mutations including:
    a. Types of mutations and genes
    b. Phenotypic variation within same gene
2. Broad-reaching advances in understanding the molecular causes of health and disease
    a. Within each nano-rare patient:
        i. Nano-rare patients uniquely have a single major variable resulting in a profound change in phenotype
        ii. Evaluate molecular effects treating a genetic disease with a targeted treatment
    b. Across nano-rare patients:
        i. Evaluate performance of ASOs on specific molecular or phenotypic effects
3. Enabling broad access to nano-rare patients regardless of means
    a. An important consideration for diversity and equity

Through support for the clinical treatment of a nano-rare patient in California, CIRM has the opportunity to impact the life of that single patient and their family, but to advance the knowledge and understanding of health and disease that will extend far beyond state lines and that single patient.