November 15, 2022

Dear supporters, partners, patients and families,

I led the creation of ASO technology, a remarkable, efficient and cost-effective platform that has facilitated the establishment of n-Lorem, a nonprofit foundation designed to provide experimental ASO medicines to appropriate nano-rare patients for free, for life. At n-Lorem, we benefit from this technology and the guidance that FDA has issued for the treatment of nano-rare patients.

Though the discovery and development of ASOs may sound simple, it is not. It requires significant expertise, knowledge, experience and automation that n-Lorem has. While I applaud the motivation of academic investigators who want to bring benefit to their patients with experimental ASOs, ASOs are complex molecules that require rigid selection criteria and careful consideration of dosing parameters. At n-Lorem, we are open to collaborations and encourage all academic investigators to work with us to take advantage of our knowledge and experience. Furthermore, the clinical administration of experimental ASOs must be done professionally by investigators knowledgeable about ASOs who have significant experience in the develop of experimental medicines.

Recently, information has been presented publicly describing serious adverse events described as normal pressure hydrocephalus (NPH) in two infants treated with a PS 2' MOE ASO. PS 2' MOE is a chemical modification discovered and developed by my lab that provides favorable drug properties to antisense molecules, but is now used broadly in designing ASO therapies. The ASO in question was not developed by n-Lorem, but given the seriousness of this event and in an effort to provide as much guidance to our investigators as possible, we issued a safety update to our investigators making them aware of this event earlier this summer.

As described in the safety update we distributed to our investigators, treating physicians and in scientific meetings, the PS 2'MOE ASO (the causal ASO) associated with these adverse events was discovered and developed independently by an academic investigator. Reviews by experts in ASO technology of the preclinical testing procedure and the ASO that caused the adverse events suggested that n-Lorem's rigid criteria would have eliminated the sub-optimal ASO that led to NPH during the discovery and development process The causal ASO was then dosed more frequently and at higher doses than recommended by n-Lorem.

We regret that these events happened. Today, we are confident that appropriate preclinical testing consistent with current guidelines, adherence to strict minimal criteria for ASO performance and appropriate dosing in the clinic should sufficiently mitigate risk for such adverse events in the future.

Sincerely,

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