IONIS® InBrief
27 December 2021

Ionis initiates HALOS clinical study of Angelman syndrome

Phase 1 / 2 a study will evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of multiple ascending doses of ION582 in patients with Angelman syndrome

In December 2021, Ionis launched the clinical process that the company hopes will one day deliver therapeutic benefit to people living with Angelman syndrome (AS), a rare and devastating neurodevelopmental disease. HALOS is a Phase 1 / 2 a, open-label dose-escalation study of ION582, an investigational antisense medicine being developed to treat AS. The study will enroll up to 44 participants to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics with multiple ascending doses of ION582.

Angelman syndrome is caused by a mutation in the UBE3A gene, resulting in a decrease in UBE3A protein in neurons. ION582 is designed to upregulate UBE3A mRNA and restore endogenous UBE3A protein expression by binding to a non-coding antisense RNA that suppresses the expression of UBE3A.

The ION582 program is partnered with Biogen, which has an option to license the drug.

AS affects an estimated 1 in 12,000 to 20,000 people globally. It is estimated that 35,000 people are diagnosed with AS in the U.S. and 30,000 in the European Union each year. Currently, there are no curative or disease-modifying therapies for Angelman syndrome. Today, approved treatments only address symptoms of AS, such as epilepsy, gastroesophageal reflux disease, sleep and behavior disturbances and constipation.

KEY TAKEAWAY

"ION582 increases expression of the UBE3A protein in neurons through a unique mechanism that exploits the versatility of antisense technology to target a long non-coding RNA. Initiation of the HALOS study is the first important clinical step towards bringing an effective, disease-modifying therapy to thousands of patients who are living with Angelman syndrome."

- C. Frank Bennett, Ph.D., executive vice president, chief scientific officer and franchise leader for neurological programs at Ionis

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What is Angelman syndrome?

AS results from the deficient function or deletion of the maternal UBE3A allele. Consequently, deficient expression or function of the maternal UBE3A allele results in neuronal-specific dysfunction.

AS is characterized by profound, lifelong neurodevelopmental disability. It manifests during the first year of life and indicates an early deviation from typical development. Children with AS characteristically start to miss major developmental milestones like talking and walking. All AS patients experience language, cognitive and motor impairments. In addition, a vast majority of AS patients (>85%) develop severe seizures and behavioral issues.

The disease emerges without standard warning signs. In utero development, neurological exam at birth, and structural brain imaging all appear normal. This severe neurodevelopmental disorder is not degenerative but relatively stable across a patient's lifespan. Thus, patients with AS typically have a normal life span in a severely disabled condition.

HALOS Study (NCT05127226)

HALOS is a Phase 1 / 2 a, open-label dose-escalation study of ION582 enrolling up to approximately 44 participants. Following a screening period of up to 4 weeks, eligible participants will receive intrathecal (IT) injections of ION582. Participants will be followed for up to 32 weeks after dosing.

To be included in the study, a participant must have a diagnosis of Angelman syndrome and a documented genetic confirmation of UBE3A deletion or mutation genotype.

For additional information about the HALOS study, including the study design and endpoints visit clinicaltrials.gov.