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Rugonersen Development Update: First Participant Dosed in the Phase 3 BEACON Trial

Dear Members of the Angelman syndrome community,

We are pleased to share an important milestone for rugonersen:

The first participant has been dosed in the Phase 3 BEACON clinical trial.

This marks an important step forward in our efforts to evaluate rugonersen as a potential disease-modifying treatment for individuals living with Angelman syndrome. We are deeply grateful to the participant and family who chose to take this first step, as well as to the investigators, study teams, and patient organizations whose partnership has made this possible. While there is still important work ahead, today marks meaningful progress toward our shared goal of bringing a potential novel treatment to the Angelman syndrome community.

About the Phase 3 Trial (BEACON)

BEACON is designed as a randomized, double-blind, sham-controlled, multi-center, Phase 3 clinical trial to evaluate the efficacy and safety of intrathecally (IT) administered rugonersen compared with a sham procedure in pediatric and adult participants with Angelman syndrome.

The trial is expected to:

- Enroll approximately 165 individuals aged 1–50 years with a genetically and clinically confirmed diagnosis of Angelman syndrome (mutation or deletion)
- Randomize participants 1:1 to either rugonersen or the sham control arm
- Evaluate the impact of rugonersen on clinically relevant outcomes, including cognition, expressive communication, and other key domains
- Evaluate the safety profile of rugonersen

The BEACON trial consists of two parts. Part 1 includes screening, a 48-week double-blind treatment period, and follow-up through Week 60. During this phase, participants will be randomly assigned to receive either rugonersen or sham treatment, and neither families nor trial staff will know which treatment the participant is receiving.

Participants who complete Part 1 may then enter Part 2, an approximately 2 year open-label extension (OLE). In the OLE, all participants will receive rugonersen every 12 weeks, regardless of the treatment assignment they received during the double-blind portion of the trial. Total participation in the trial may therefore extend to approximately 3 years.

About Rugonersen

Rugonersen is an investigational medicine designed to target the underlying cause of Angelman syndrome rather than just treating its symptoms. It works by helping to switch on the healthy copy of the UBE3A gene that is naturally inherited from the father but is normally turned off. By reactivating this gene, rugonersen aims to increase production of the UBE3A protein, which is important for brain function and development. Researchers hope that restoring UBE3A activity may improve brain function and support learning, communication, movement, and other areas affected in individuals with Angelman syndrome.

Our commitment to the Angelman syndrome community

We recognize the urgency felt by families and caregivers and the need for effective therapies. There are currently no approved disease-modifying treatments for Angelman syndrome, underscoring the importance of continued research in this field.

We are deeply grateful to all individuals living with Angelman syndrome, their families and caregivers, patient advocacy organizations, and trial teams.
Your partnership is essential to advancing research and making progress toward new treatment options.

Next Steps

Enrollment in the BEACON trial is ongoing, and additional clinical sites are expected to begin enrolling participants over the coming months.

As the trial progresses, we remain committed to providing updates on important milestones as appropriate. We encourage families interested in learning more about BEACON to speak with their healthcare provider or contact a participating trial site to determine whether the trial may be appropriate.

Thank you for your continued support and partnership as we work together to advance research for Angelman syndrome.

Sincerely,

Brenda Vincenzi

Brenda Vincenzi, M.D.
Chief Medical Officer
Oak Hill Bio

Q&A

What is rugonersen and how does it work?

Rugonersen is an investigational antisense oligonucleotide (ASO) designed to target the UBE3A-antisense transcript (UBE3A-ATS). In Angelman syndrome (AS), the maternal UBE3A gene is not functioning properly, while the paternal copy is intact but naturally silenced in neurons. Rugonersen is designed to reduce UBE3A-ATS, which may allow the paternal UBE3A gene to become active and produce UBE3A protein in the brain. The goal is to address the underlying molecular cause of AS rather than only treating symptoms.

How is rugonersen administered and why?

Rugonersen is given by intrathecal (IT) administration, meaning it is injected into the cerebrospinal fluid (CSF) through a lumbar puncture (LP) in the lower back. This route is used because ASOs do not effectively cross the blood-brain barrier when given by mouth or standard intravenous injection. IT administration allows rugonersen to reach the central nervous system directly.

What age groups are included in the BEACON Phase 3 trial?

The BEACON Phase 3 trial plans to enroll participants aged 1 to 50 years. Approximately 135 pediatric participants aged 1–17 years and approximately 30 adult participants aged 18–50 years are expected to participate. Participants will be randomised 1:1 to the sham arm or to the rugonersen arm.

Is there a placebo included in the BEACON Phase3 trial? And what does the sham procedure look like?

The BEACON trial uses a sham-controlled design (and not a placebo) to maintain blinding and ensure unbiased assessment of outcomes.

The sham procedure is designed to closely mimic the active treatment experience, including participant preparation, positioning, procedural timing, and use of sedation or anesthesia when appropriate. During the sham procedure, a superficial needle prick at the lumbar region will be performed to simulate the active procedure and create a comparable local experience, without administration of rugonersen or placebo into the cerebrospinal fluid. Participants in the sham arm will receive two lumbar punctures without administration of placebo.

How long is the BEACON trial?

The BEACON trial has two parts. Part 1 includes screening, a 48-week double-blind treatment period, and a follow-up period through Week 60. Participants who complete Part 1 may enter Part 2, an approximately 116-week open-label extension (OLE), where all participants receive rugonersen every 12 weeks. Total participation could therefore extend to approximately 3 years.

What are the plans for the UPD and ICD genotypes?

Individuals with UPD or ICD genotypes are not included in the current Phase 3 BEACON trial. However, Oak Hill Bio recognizes the importance of these patient populations, and future trials may evaluate rugonersen in broader AS genotypes if sufficient safety and efficacy data are generated.

My family is interested in participating in BEACON. How do we enroll in the trial?

Families interested in participating in the trial may contact the trial site team or participating trial site to learn more about the trial and determine whether their loved one may be eligible. After initial contact, the trial site team will explain the study procedures, review the trial eligibility criteria, and answer any questions.

Where will the BEACON trial sites be located?

The BEACON trial is planned as a global, multicenter trial. Information regarding participating sites and trial contacts will be shared as sites become activated, and enrollment begins. Updated information will be shared through the BEACON study website (LINK), clinicaltrials.gov (LINK), patient advocacy organizations, and other trial communications (e.g. at conferences or webinars).