



July 2026

Dear Angelman Syndrome Community,

Ionis is pleased to inform you that we have completed enrollment of the pivotal study arm (Cohort 1) of our Phase 3 clinical trial of ION582 (obudanersen), REVEAL. Initial results are anticipated during the second half of 2027.<sup>1,2</sup>

Obudanersen, an antisense oligonucleotide (ASO), is an investigational medicine designed to increase UBE3A protein production in people with AS. REVEAL is designed to evaluate the efficacy and safety of obudanersen in children and adults with AS. Approximately 158 individuals with *UBE3A* mutation- or deletion-positive AS will be enrolled in REVEAL.<sup>1,2</sup>

Individuals enrolled in REVEAL are assigned to study “Cohorts” based on their age. Individuals aged 2 - <18 years old are assigned to Cohort 1, and individuals aged 18 - ≤50 years old are assigned to Cohort 2. While enrollment in Cohort 1 has been completed, participating sites continue to screen participants for Cohort 2. Ionis will update [clinicaltrials.gov](https://clinicaltrials.gov) to reflect this milestone and note which sites will continue to screen participants for Cohort 2. Once enrollment in Cohort 2 is complete, the study will be considered fully enrolled.<sup>1</sup>

REVEAL remains ongoing, with participants in both cohorts moving through the study’s double-blind control period, in which they are randomized to the control arm or the 80mg obudanersen arm. Upon completion of the double-blind control period, study participants may advance to the long-term extension period of the study, in which all participants receive 80mg obudanersen.<sup>1,2</sup>

Ionis thanks all individuals with Angelman syndrome and their families, site investigators and their staff, who continue to work tirelessly to advance clinical research studies like REVEAL. Ionis will share additional updates in the future.

Sincerely,

The Obudanersen Team

**The following is additional information you may find helpful:**

What is a pivotal study arm?

REVEAL is a pivotal study, meaning it is designed to evaluate whether a drug is both safe and effective enough to warrant approval by regulatory agencies (e.g., the U.S. Food & Drug Administration) for broader use in AS.<sup>1</sup>

Cohort 1 in REVEAL, which includes pediatric participants aged 2 to less than (<)18 years old, will serve as the pivotal population for the study, which means it will serve as the primary population to evaluate

the safety and efficacy of obudanersen. Researchers use these arms to confirm the safety and efficacy of a new drug or medical device before submitting it for regulatory approval.<sup>1</sup>

Data from Cohort 2 is similarly critically important, as it will be used alongside data from Cohort 1 to determine whether obudanersen is safe and effective in both pediatric and adult patients living with AS.<sup>1</sup>

#### When will results from REVEAL be announced?

Enrollment of Cohort 1 occurred more quickly than originally anticipated. The estimated primary study end date on [clinicaltrials.gov](https://clinicaltrials.gov) has been updated to July 2027 (previously August 2027). Results will be announced after that date, when available. Study timelines are subject to change.<sup>1</sup>

#### Where can someone interested in learning more about Cohort 2 go for more information?

Cohort 2 is limited to only individuals with Angelman syndrome who are mutation and deletion positive and are 18 - ≤50 years old at the time of enrollment. Individuals interested in learning more about participating in a clinical trial should speak with their doctor. Additional information about REVEAL is available online at <https://clinicaltrials.gov/study/NCT06914609>.<sup>1</sup>

#### Why aren't all REVEAL sites enrolling people into both Cohorts?

Before activation, each site was required to determine whether it had the expertise and infrastructure to enroll participants in Cohort 1, Cohort 2, or both. We will continue to update [clinicaltrials.gov](https://clinicaltrials.gov) to indicate which REVEAL sites are recruiting participants into Cohort 2.

#### What is the status of CHAMPION, Ionis' study of obudanersen in UPD/ID-positive AS patients?

In November 2025, Ionis announced plans to open a clinical trial of obudanersen in people with Angelman syndrome caused by UPD (uniparental disomy) and ID (imprinting defect). Ionis has been advancing plans for this potential trial, including seeking input from caregivers to UPD/ID-positive patients, physicians, and regulators. We anticipate opening the trial before the end of 2026. Additional information will be shared in the future.<sup>4</sup>

—

The [Angelman Syndrome Foundation](#) and the [Foundation for Angelman Syndrome Therapeutics \(FAST\)](#) are community organizations that provide resources and support to patients, caregivers, and others impacted by Angelman syndrome. For more information about Ionis, visit [www.ionis.com](http://www.ionis.com) or email [padvocacy@ionis.com](mailto:padvocacy@ionis.com).

References: 1. [Clinicaltrials.gov. NCT06914609](https://clinicaltrials.gov/study/NCT06914609). Accessed June 22, 2026, 2. Explore our pipeline. Accessed June 22, 2026. <https://ionis.com/science-and-innovation/pipeline>., 3. [Clinicaltrials.gov. NCT05127226](https://clinicaltrials.gov/study/NCT05127226). Accessed June 22, 2026., 4. Junge, C. Update on the Ionis Development Program for Angelman Syndrome. Presentation at FAST Summit 2025. Orlando, Florida.

PA-US-AS-260002 v1 07/2026