Ionis completes enrollment in pivotal cohort of the Phase 3 REVEAL study evaluating obudanersen in Angelman syndrome

July 6, 2026

- Topline data from REVEAL anticipated in 2H 2027 -

CARLSBAD, Calif.--(BUSINESS WIRE)--Jul. 6, 2026-- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today announced that it has completed enrollment in the pivotal cohort (Cohort 1) of the global Phase 3 REVEAL study evaluating obudanersen (ION582), an investigational RNA-targeted medicine for people living with Angelman syndrome (AS), a serious and rare neurodevelopmental disorder associated with significant impairments in communication, physical function and cognition. The pivotal cohort enrolled 136 participants aged 2 to < 18 years old with a confirmed clinical diagnosis of AS with genetic confirmation of either a UBE3A deletion or UBE3A mutation. The adult cohort (Cohort 2) comprised of participants aged 18 to ≤ 50 years old living with AS is expected to complete enrollment in the third quarter of 2026. Topline data from the REVEAL study is expected in the second half of 2027.

"Completion of enrollment in the pivotal cohort of REVEAL marks an important step towards a potential disease modifying treatment for people living with this serious and complex neurological condition, for which there are no approved medicines," said Holly Kordasiewicz, Ph.D., executive vice president, chief development officer, Ionis. "Guided by input from the Angelman community, REVEAL was intentionally designed to evaluate obudanersen across a broad range of people living with Angelman syndrome, reflecting the real-world diversity of this condition. We are deeply grateful to the entire Angelman syndrome community, especially the participants and their families, whose partnership made this achievement possible."

REVEAL (NCT06914609) is a global, randomized, double-blind, controlled Phase 3 study that will enroll approximately 158 individuals with a confirmed clinical diagnosis of AS with genetic confirmation of either a UBE3A deletion or UBE3A mutation. REVEAL is comprised of two cohorts. Cohort 1 (pivotal cohort) includes pediatric participants aged 2 to < 18 years old and serves as the population for evaluation of primary and secondary endpoints. Cohort 2 (adult cohort) will include adult participants aged 18 to ≤ 50 years old. The primary endpoint is improvement in expressive communication as assessed by the Bayley Scales for Infant and Toddler Development-4 (Bayley-4), an objective and direct clinician-administered assessment of clinical functioning. Deficits in expressive communication are reported to be the symptoms most meaningful to caregivers of people with AS. Secondary endpoints include overall disease severity, cognition, communication, sleep, motor functioning and daily living skills, in addition to other exploratory endpoints.

Ionis also plans to advance obudanersen into the Phase 3 CHAMPION study to evaluate obudanersen in people with AS who have uniparental disomy (UPD) or imprinting defect (ID) genotypes. The CHAMPION study is on track to initiate before the end of 2026.

About obudanersen (ION582)

Obudanersen (ION582) is an investigational RNA-targeted antisense medicine designed to inhibit the expression of the UBE3A antisense transcript (UBE3A-ATS) and increase production of UBE3A protein, for the potential treatment of Angelman syndrome (AS). The U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) granted Orphan Drug designation to obudanersen for the treatment of AS. Additionally, the FDA granted Fast Track and Rare Pediatric designations to obudanersen for the treatment of AS.

About Angelman Syndrome (AS)

AS is a rare, genetic neurological disease that affects an estimated 1 in 21,000 people worldwide and is caused by the loss of function of the maternal *UBE3A* gene. AS typically presents in infancy and is characterized by profound intellectual disability, balance issues, motor impairment and debilitating seizures. Most people with AS are unable to speak. Individuals with AS have a normal lifespan but require complete care from a caregiver. Some symptoms can be managed with existing medicines; however, there are no approved disease modifying therapies.

About Ionis Neurology

Ionis has been at the forefront of discovering and developing leading neurological disease medicines, including SPINRAZA® (nusinersen), the first approved treatment for spinal muscular atrophy, WAINUA® (eplontersen), a medicine to treat hereditary transthyretin-mediated amyloid polyneuropathy (ATTRv-PN), and QALSODY® (tofersen) for SOD1-ALS. The clinical-stage portfolio

includes 13 investigational medicines, of which six are wholly owned by Ionis. Ionis' investigational portfolio includes medicines for which there are few or no disease modifying treatments, such as rare diseases including Alexander disease, Angelman syndrome, prion disease, multiple system atrophy and Huntington’s disease, as well as more common conditions such as Alzheimer's disease.

About Ionis Pharmaceuticals, Inc.

For more than three decades, Ionis has invented medicines that bring better futures to people with serious diseases. Ionis currently has marketed medicines and a leading pipeline in neurology, cardiometabolic disease and select areas of high patient need. As the pioneer in RNA-targeted medicines, Ionis continues to drive innovation in RNA therapies in addition to advancing new approaches in gene editing. A deep understanding of disease biology and industry-leading technology propels our work, coupled with a passion and urgency to deliver life-changing advances for patients. To learn more about Ionis, visit Ionis.com and follow us on X (Twitter), LinkedIn and Instagram.

Ionis Forward-looking Statements

This press release includes forward-looking statements regarding Ionis' business and the therapeutic and commercial potential of obudanersen (ION582), our commercial medicines, additional medicines in development and technologies and our expectations regarding development and regulatory milestones. Any statement describing Ionis' goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties including those inherent in the process of discovering, developing and commercializing medicines that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such medicines. Ionis' forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Although Ionis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Ionis. Except as required by law, we undertake no obligation to update any forward-looking statements for any reason. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Ionis' programs are described in additional detail in Ionis' annual report on Form 10-K and most recent Form 10-Q for the year ended December 31, 2025, which are on file with the Securities and Exchange Commission. Copies of these and other documents are available from the Company.

In this press release, unless the context requires otherwise, "Ionis," "Company," "we," "our" and "us" all refer to Ionis Pharmaceuticals and its subsidiaries.

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