Ionis Partner Biogen Presents Phase 2 CELIA Data at AAIC Demonstrating Meaningful Clinical Outcomes and Robust Tau Reduction with Diranersen in Early Alzheimer's Disease

July 14, 2026

*- **Clinical outcomes:** Diranersen demonstrated efficacy across all studied doses at 18 months, with consistent results across multiple prespecified clinical endpoints; the 60 mg dose showed the strongest response with slowing of clinical decline on the cognitive endpoints—42% on ADAS-Cog13 and 50% on MMSE—alongside a 26% slowing on CDR-SB ·*

*- **Biomarker response:** Diranersen is the first tau-directed therapy to demonstrate robust reductions in both CSF total tau, with mean reductions of 50–65%, and brain tau pathology, as measured by PET, across all studied doses in a Phase 2 study -*

*- **Dose response:** CDR-SB results favored diranersen versus placebo across all studied doses; higher doses were not associated with greater slowing of decline -*

*- **Mechanism of action:** Distinct from other tau-lowering approaches, diranersen targets MAPT mRNA to reduce the production of all tau isoforms, lowering both intracellular and extracellular tau protein -*

CARLSBAD, Calif.--(BUSINESS WIRE)--Jul. 14, 2026-- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today announced that its partner, Biogen, shared data from the Phase 2 CELIA study evaluating diranersen, an investigational antisense oligonucleotide (ASO) therapy targeting tau, in individuals with early Alzheimer's disease. The data, presented at the Alzheimer's Association International Conference (AAIC) 2026, expand upon previously reported topline results and demonstrate a combination of meaningful clinical efficacy and robust biomarker effects, providing Phase 2 proof of concept for diranersen's tau-directed mechanism of action. Based on the growing and consistent body of evidence from the Phase 1b and Phase 2 studies, Biogen plans to advance diranersen into confirmatory Phase 3 development.

"The CELIA data presented at AAIC provide important new insights into the potential of diranersen to markedly lower all forms of tau and meaningfully improve outcomes in early Alzheimer's disease," said Holly Kordasiewicz, Ph.D., executive vice president, chief development officer, Ionis. "We are proud to have discovered diranersen and to partner with Biogen as this program advances into Phase 3 development. This progress reflects the strength of our RNA-targeted platform and deep expertise advancing innovative therapies for some of the most challenging neurological diseases."

Diranersen demonstrated efficacy across all studied doses at 18 months, with consistent efficacy across multiple prespecified secondary endpoints, including the Clinical Dementia Rating–Sum of Boxes (CDR-SB), a global measure of cognition and daily function; ADAS-Cog13 and MMSE, measures of cognition; modified iADRS and ADCOMS, composite measures of cognition, function, and disease progression; as well as the individual cognitive and functional domains of CDR-SB. Diranersen 60 mg administered intrathecally every six months (n=60) showed the strongest response at 18 months. Compared with placebo (n=115), diranersen 60 mg demonstrated slowing of clinical decline by 0.54 points (26%) on CDR-SB; 42% on ADAS-Cog13; 50% on MMSE; 30% on modified iADRS; and 23% on ADCOMS. The majority of these endpoint differences achieved nominal statistical significance compared with placebo.

Clinical effects were also observed in the other studied dose regimens. Compared with placebo, diranersen 115 mg administered intrathecally every six months (n=115) and diranersen 115 mg administered intrathecally every three months (n=116) demonstrated slowing of clinical decline by 0.28 and 0.18 points (14% and 9%) on CDR-SB; 32% and 29% on ADAS-Cog13; 34% and 38% on MMSE; 29% and 18% on modified iADRS; and 21% and 7% on ADCOMS, respectively. At 18 months, no separation from placebo was observed across dose groups on ADCS-ADL-MCI, a measure of daily functioning, and longer-term follow-up continues to assess whether a longer duration of diranersen therapy impacts this endpoint. Of note, while ADCS-ADL-MCI results were inconsistent across dose regimens, slowing of functional decline based on the functional domains of CDR-SB favored diranersen across all studied doses.

CELIA was designed with a primary endpoint of dose response on CDR-SB at 18 months to investigate whether higher doses of diranersen could provide greater clinical benefit. As previously disclosed, this was not observed, and the study did not meet its primary endpoint.

Diranersen demonstrated target engagement and robust reductions in cerebrospinal fluid (CSF) total tau across all studied doses, with mean reductions of 50–65% from baseline. In the tau PET imaging substudy (n=131), decreases from baseline were seen across all evaluated brain regions for all diranersen doses. Diranersen is the first tau-directed therapy to demonstrate reductions in

both CSF total tau and brain tau pathology, as measured by PET, across all studied doses in a Phase 2 study.

Diranersen was generally well tolerated. During the placebo-controlled period, most participants who experienced adverse events had events that were mild or moderate in severity, non-serious, and did not result in treatment discontinuation or study withdrawal. The most frequent adverse events were procedural pain, post-lumbar puncture syndrome, and confusional state. Most adverse events of confusional state occurred within a few days of dosing and resolved within a week. Among participants who completed the placebo-controlled period, more than 90% elected to continue into the extension study. Amyloid-related imaging abnormalities (ARIA) are not anticipated with diranersen based on its tau-targeting mechanism of action, and the results from CELIA are consistent with that expectation.

The study enrolled a population representative of early Alzheimer's disease, with baseline characteristics generally balanced across treatment groups. Participants had a mean age of 68 years, 51% were female, and 60% were classified as having mild cognitive impairment, with 40% having mild Alzheimer's disease dementia. ApoE4 carriers represented approximately 69% of participants, including 23% homozygotes.

Additional analyses and data from CELIA and the ongoing long-term extension study will be presented at future scientific conferences.

About diranersen (IONIS-MAPTrx/BIIB080)

Diranersen (IONIS-MAPTrx/BIIB080) is an investigational antisense oligonucleotide (ASO) therapy designed to target microtubule-associated protein tau (MAPT) mRNA to reduce the production of tau protein. Unlike many investigational approaches that have focused on targeting extracellular tau, diranersen is designed to reduce both intracellular and extracellular tau.

Diranersen is being investigated as a potential treatment for early Alzheimer's disease. In 2025, the U.S. Food and Drug Administration (FDA) granted Fast Track designation to diranersen for the treatment of Alzheimer's disease.

In December 2019, Biogen exercised a license option with Ionis Pharmaceuticals and obtained a worldwide, exclusive, royalty-bearing license to develop and commercialize diranersen. Diranersen was discovered by Ionis.

About the CELIA Study

CELIA is a global Phase 2 randomized, double-blind, placebo-controlled, dose-ranging study evaluating the efficacy, safety, and tolerability of diranersen in individuals with early Alzheimer's disease. The study enrolled 416 participants with mild cognitive impairment due to Alzheimer's disease or mild Alzheimer's disease dementia. All participants enrolled in CELIA had not previously received anti-amyloid therapy.

The study evaluated three doses of diranersen administered intrathecally over an 18-month placebo-controlled treatment period: 60 mg every six months, 115 mg every six months, and 115 mg every three months.

The primary endpoint of CELIA was assessment of dose response for change from baseline on the Clinical Dementia Rating–Sum of Boxes (CDR-SB) at Week 76. Secondary and exploratory endpoints included additional clinical, biomarker, and imaging measures, including cerebrospinal fluid tau biomarkers and tau positron emission tomography (PET). Additional information on the study design is available in the ClinicalTrials.gov listing for the CELIA study.

An ongoing long-term extension (LTE) study is continuing to evaluate the long-term safety, tolerability, and durability of diranersen's clinical benefit in early Alzheimer's disease.

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 diranersen (IONIS-MAPTrx), 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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