Diranersen demonstrates increasing clinical benefit at two years in early Alzheimer's disease

November 17, 2026

- Diranersen slowed clinical decline by 38% on CDR-SB at two years (Week 96) with the 60 mg twice-yearly regimen, corresponding to a 1.09-point treatment difference -

- Greater slowing of clinical decline across 5 of 6 measures at two years compared with 18 months (Week 76) in the 60 mg dose group -

- Clinical benefits were observed across all doses studied, with the 60 mg dose group showing compelling efficacy and a favorable benefit-risk profile -

- Data presented at the Clinical Trials on Alzheimer's Disease (CTAD) conference –

CARLSBAD, Calif.--(BUSINESS WIRE)--Nov. 17, 2026-- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today announced that its partner, Biogen, shared new data from the Phase 2 CELIA study showing increasing clinical benefit of diranersen, an investigational antisense oligonucleotide (ASO) therapy targeting tau, in people living with early Alzheimer's disease at two years (Week 96). Results presented at the Clinical Trials on Alzheimer's Disease (CTAD) 2026 conference showed slowing of clinical decline across measures of cognition, function and disease progression, with the 60 mg twice-yearly regimen showing the largest treatment effects at two years.

“The diranersen data presented at CTAD underscore the potential of our RNA-targeted technology to achieve meaningful reductions in tau and reinforce the promise of tau-lowering as a therapeutic approach for people living with early Alzheimer’s disease,” said Holly Kordasiewicz, Ph.D., executive vice president, chief development officer, Ionis. “The sustained and deepening clinical benefits are encouraging and we are proud to partner with Biogen.”

At two years, analyses showed that diranersen continued to slow clinical decline across measures of cognition, function and disease progression. Clinical benefits were observed across all doses studied, with the 60 mg twice-yearly regimen showing the largest treatment effects at two years. Diranersen was generally well tolerated through two years, with no new safety signals observed.

Clinical outcomes with the 60 mg twice-yearly regimen (n=60) versus participants originally randomized to placebo (n=115)	**Week 76**	**Week 96**
CDR-SB	26%	38%*
ADAS-Cog13	42%	54%
MMSE	50%	38%
ADCS-ADL-MCI	0%	30%
ADCOMS	23%	38%
Modified iADRS	30%	46%

* Corresponding to a 1.09-point treatment difference on CDR-SB at Week 96

The two-year analyses were derived from the ongoing open-label extension phase of CELIA. Treatment effects were calculated by comparing participants who received diranersen during the placebo-controlled phase of the study and remained on the same dose through two years with participants who were initially assigned to placebo and transitioned into the extension phase. At Week 96, participants in the placebo group had received either no doses or a single dose of diranersen following their transition into the extension phase, providing a placebo-equivalent comparator. All participants in the extension phase are expected to receive diranersen as the study progresses.

Alongside the two-year results, Biogen presented new 18-month placebo-controlled clinical and biomarker findings from CELIA that further support the effects of diranersen. At 18 months, the twice-yearly 60 mg diranersen sub-group analysis showed preferential efficacy in memory, orientation, and executive function. Diranersen also robustly reduced tau PET signal broadly across the brain, CSF p-tau181, and plasma p-tau217.

These data build on previously reported results from the Phase 2 CELIA study and further support the continued development of

diranersen for people living with early Alzheimer's disease.

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 ZANVASTRO™ (zilganersen), the only approved treatment for Alexander disease, 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 11 investigational medicines, of which seven 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 Angelman syndrome, prion disease and multiple system atrophy, as well as more common conditions like 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, 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 for the year ended December 31, 2025 and most recent Form 10-Q, 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

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Source: Ionis Pharmaceuticals, Inc