Ionis partner Biogen announces topline results from Phase 2 CELIA study of diranersen (BIIB080): first study to show reduction in tau pathology and cognitive benefit in patients with early Alzheimer's disease

May 14, 2026

- Based on the strength of the biomarker and efficacy data, Biogen plans to advance diranersen to registrational development; CELIA did not meet its primary endpoint assessing dose response -

- Robust reductions in tau pathology were observed across all studied doses, with results generally consistent with those observed in the Phase 1b study -

- Pre-specified analyses of cognitive endpoints demonstrated slowing of clinical decline across all studied doses, particularly at the lowest dose -

- The safety and tolerability profile of diranersen was generally consistent with the Phase 1b study -

- Data will be presented at the Alzheimer's Association International Conference (AAIC) 2026 and other upcoming scientific congresses -

CARLSBAD, Calif.--(BUSINESS WIRE)--May 14, 2026-- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today announced that its partner, Biogen, shared compelling topline results from the Phase 2 CELIA study evaluating diranersen (IONIS-MAPT$_{Rx}$/BIIB080), an investigational antisense oligonucleotide (ASO) therapy targeting tau, in individuals with early Alzheimer's disease (AD). The CELIA results provide the first evidence from a randomized Phase 2 study of a tau-directed therapy demonstrating both robust biomarker impact and cognitive benefit in early AD.

"We are highly encouraged by the topline results from CELIA, which underscore the potential of targeting tau to meaningfully impact patient outcomes in early Alzheimer's disease," Holly Kordasiewicz, Ph.D., executive vice president, chief development officer, Ionis. "These findings represent an important advancement for the field and underscore the impact of Ionis' growing neurology portfolio, which now includes 13 medicines in clinical development including six that are wholly owned. We're proud to have discovered diranersen and are deeply grateful to everyone who made this research possible."

Pre-specified analyses of cognitive endpoints demonstrated slowing of clinical decline across all studied doses, particularly in participants receiving the lowest dose of diranersen, 60 mg administered every 24 weeks. Diranersen also demonstrated robust reductions in both cerebrospinal fluid (CSF) tau and tau pathology, as measured by positron emission tomography (PET), across all studied doses, with reductions maintained throughout the dosing period. CELIA did not meet its primary endpoint assessing dose response for change from baseline on the Clinical Dementia Rating–Sum of Boxes (CDR-SB) at Week 76.

"In CELIA, we believe we have seen an unprecedented and compelling confluence of efficacy and biomarkers results from a tau-directed agent in a randomized early Alzheimer's disease study," said Priya Singhal, M.D., M.P.H., Executive Vice President and Head of Development at Biogen. "We are excited by these Phase 2 data, which give us the confidence to advance diranersen to registrational development. We look forward to engaging with regulators and the broader Alzheimer's disease community on next steps. I would like to thank the patients, families, investigators, and study teams who participated in this pioneering study."

The safety and tolerability profile of diranersen across all studied doses was generally consistent with the Phase 1b study and the known profile of diranersen to date. The incidence of adverse events (AEs) was comparable across dose groups, with a higher incidence of serious adverse events (SAEs) observed at the highest dose studied.

CELIA is a pioneering study evaluating diranersen, a first-in-class investigational ASO designed to reduce the production of tau protein at its source in early AD. While tau plays an important role in the normal function of brain cells, in AD, abnormal tau can accumulate and form intracellular tangles that contribute to neurodegeneration and cognitive decline. Unlike many investigational approaches that have focused on targeting extracellular tau, diranersen is designed to reduce both extracellular and intracellular tau.

About diranersen (IONIS-MAPT$_{Rx}$/BIIB080)

Diranersen (IONIS-MAPT$_{Rx}$/BIIB080) is an investigational antisense oligonucleotide (ASO) therapy designed to target microtubule-associated protein tau (MAPT) mRNA to reduce the production of tau protein. Abnormal accumulation of tau in the brain is a

hallmark of Alzheimer's disease (AD) associated with neurodegeneration and cognitive decline.

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

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 (AD). The study enrolled 416 participants with mild cognitive impairment due to AD or mild AD dementia. All participants enrolled in CELIA had not previously received anti-amyloid therapy.

The study evaluated three doses of diranersen administered intrathecally over a 76-week placebo-controlled treatment period: 60 mg every 24 weeks, 115 mg every 24 weeks and 115 mg every 12 weeks.

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 CELIA 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 in early AD.

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 Angelman syndrome, prion disease, multiple system atrophy, Huntington's disease and Alexander disease, as well as more common conditions such as Alzheimer's disease.

About Ionis Pharmaceuticals, Inc.

For 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-MAPT$_{Rx}$/BIIB080), 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.

View source version on businesswire.com: https://www.businesswire.com/news/home/20260514986673/en/

Ionis Investor Contact:
D. Wade Walke, Ph.D.
IR@ionis.com 760-603-2331

Ionis Media Contact:
Hayley Soffer
media@ionis.com 760-603-4679

Source: Ionis Pharmaceuticals, Inc.