Ionis announces zilganersen New Drug Application for Alexander disease (AxD) accepted by FDA for Priority Review

March 23, 2026

– PDUFA date set for September 22, 2026 –

CARLSBAD, Calif.--(BUSINESS WIRE)--Mar. 23, 2026-- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today announced that the U.S. Food and Drug Administration (FDA) has accepted for Priority Review the New Drug Application (NDA) for zilganersen, an investigational RNA-targeted medicine for Alexander disease (AxD), a rare, progressive and often fatal neurological condition. The FDA has set a Prescription Drug User Fee Act (PDUFA) target action date of September 22, 2026.

"Alexander disease is a devastating condition, commonly resulting in progressive motor and cognitive dysfunction, loss of independence and is often fatal. There are no approved disease-modifying treatments, underscoring the significant unmet need in this community," said Brett Monia, Ph.D., chief executive officer, Ionis. "Priority Review designation underscores the urgent need for treatment options and will enable us to bring zilganersen to patients as quickly as possible. If approved, zilganersen will be the first and only treatment for Alexander disease, marking a breakthrough for patients. It would also mark Ionis' first independent commercial launch in neurology, an important milestone that strengthens our neurology franchise and supports our goal to deliver a steady cadence of transformational medicines to people with serious diseases."

The NDA and Priority Review designation were based on results from the pivotal study of zilganersen in children and adults living with AxD. In the study, zilganersen 50 mg demonstrated statistically significant and clinically meaningful stabilization on the primary endpoint of gait speed as assessed by the 10-Meter Walk Test (10MWT) compared to control at week 61 (least square mean difference 33.3%, p=0.0412) with favorable safety and tolerability. Results across key secondary and exploratory endpoints evaluating adaptive function, communication, GI symptoms, sleep and seizures also consistently favored zilganersen. New, additional data from the pivotal study will be presented at the 2026 American Academy of Neurology (AAN) annual meeting in Chicago, IL.

Priority Review designation is granted to marketing applications for medicines that, if approved, would provide a significant improvement in the safety or effectiveness of the treatment, prevention or diagnosis of a serious condition, with the expectation of the FDA taking action within six months, compared to 10 months under standard review. The FDA previously granted zilganersen Breakthrough Therapy, Orphan Drug and Rare Pediatric Disease designations.

About the Zilganersen Study

The global, multicenter, randomized, double-blind, controlled, multiple-ascending dose (MAD) Phase 1-3 study (NCT04849741) enrolled 54 participants with Alexander disease (AxD) between the ages of 1.5 and 53 years across 13 sites in eight countries. Most participants in the study were children, reflecting the early onset and severe progression of AxD in pediatric populations. Participants were randomized in a 2:1 ratio to receive zilganersen or control for a 60-week double-blind treatment period. The study included two dose cohorts, 25 mg and 50 mg, with the 50 mg dose cohort analyzed as the pivotal dose cohort, with dosing every 12 weeks. At 60 weeks, all eligible participants transitioned into an open-label treatment period, followed by a 120-week open-label, long-term extension treatment period, during which participants in the 25 mg dose cohort moved to the 50 mg dose cohort, and finally a 28-week post-treatment follow-up period. The primary endpoint is percent change from baseline in gait speed as assessed by the 10-Meter Walk Test (10MWT), an assessment of functional mobility, at the end of the double-blind treatment period. Key secondary endpoints include patients' self-identified Most Bothersome Symptom (MBS) Score, change from baseline in Patient Global Impression of Severity (PGIS) Score and Patient Global Impression of Change (PGIC) Score and Clinician Global Impression of Change (CGIC) Score at the end of the double-blind treatment period.

About Zilganersen

Zilganersen is an investigational antisense oligonucleotide medicine being evaluated as a treatment for people with Alexander disease (AxD). Zilganersen is designed to inhibit production of excess glial fibrillary acidic protein (GFAP) that accumulates because of disease-causing variants in the *GFAP* gene. The U.S. Food and Drug Administration (FDA) granted zilganersen Breakthrough Therapy, Orphan Drug and Rare Pediatric Disease designations. In addition, the European Medicines Agency (EMA) granted zilganersen Orphan Drug designation.

About Alexander Disease (AxD)

AxD is a rare, progressive and often fatal neurological disease that occurs in approximately 1 per 1 to 3 million people worldwide

and affects a type of cell in the brain called astrocytes. Astrocytes have multiple roles in the brain to support neurons and oligodendrocytes, including maintenance of the myelin sheath that protects nerve fibers. AxD is caused by disease-causing variants in the glial fibrillary acidic protein (*GFAP*) gene and is generally characterized by progressive neurological deterioration resulting in loss of functional mobility, loss of independence and the inability to control muscles for large movements, swallowing and airway protection, though symptoms can vary depending on age of onset. AxD usually leads to death within 14-25 years after symptom onset. There are no approved disease-modifying medicines.

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 12 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 zilganersen, 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, which is 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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