ZANVASTRO™ (zilganersen) approved by the FDA as the first and only disease modifying treatment for Alexander disease (AxD) in pediatric and adult patients

September 3, 2026

- Provides a clinically meaningful impact on motor function and a favorable impact on other symptoms seen in AxD, an ultra-rare, progressive and often fatal neurological disorder -

- Priority Review Voucher (PRV) awarded in conjunction with approval -

- ZANVASTRO marks Ionis' first independent launch from its industry-leading neurology pipeline and second independent launch this year -

– Ionis to host webcast on Friday, Sept. 4 at 10:00 a.m. ET –

CARLSBAD, Calif.--(BUSINESS WIRE)--Sep. 3, 2026-- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today announced that the U.S. Food and Drug Administration (FDA) has approved ZANVASTRO™ (zilganersen) for the treatment of Alexander disease (AxD) in pediatric and adult patients. ZANVASTRO is the first and only disease modifying treatment for AxD, an ultra-rare, progressive and often fatal neurological disorder that can affect motor, cognitive, autonomic and gastrointestinal function. Until now, treatment of AxD has primarily been limited to managing symptoms. ZANVASTRO is an RNA-targeted medicine designed to address the underlying disease mechanism of AxD by reducing the production of glial fibrillary acidic protein (GFAP). ZANVASTRO 50 mg is administered quarterly as an intrathecal (IT) injection.

This press release features multimedia. View the full release here: https://www.businesswire.com/news/home/20260903826844/en/

ZANVASTRO (zilganersen) logo

"Today's approval of ZANVASTRO begins a new chapter for people living with Alexander disease and their families, who have long faced this relentlessly progressive and often fatal disease with no treatment options," said Brett P. Monia, Ph.D., chief executive officer, Ionis. "This transformative approval also marks our first independent launch from our industry-leading neurology pipeline and underscores the power of our RNA-targeted technology to address serious neurological diseases without adequate treatment options. We are proud to bring this important new treatment to this incredible community and are deeply grateful to the clinical trial participants and their families, regulators, investigators and advocates who helped make this advancement possible."

AxD affects approximately 1 in 1 to 3 million people worldwide. Initial signs of AxD can present from infancy through adulthood and may vary depending on age of onset. As AxD progresses, symptoms may include progressive motor and cognitive dysfunction, a loss of independence and the inability to control muscles for swallowing, airway protection and purposeful movements. AxD is caused by changes in the *GFAP* gene that lead to the overproduction and toxic accumulation of GFAP in astrocytes. Over time, dysfunction in astrocytes can damage neurons and myelin, which can lead to symptoms commonly associated with AxD.

"For decades, care for people living with Alexander disease has focused primarily on managing symptoms, without an option to modify the underlying cause of disease," said Amy Waldman, M.D., M.S.C.E., pediatric neurologist and lead investigator for the ZANVASTRO study at Children's Hospital of Philadelphia. "The approval of ZANVASTRO for the treatment of Alexander disease represents a significant advancement in care and opens new possibilities for patients and their families. For the first time, we can move beyond managing individual manifestations of the disease to addressing its underlying biology, with the potential to meaningfully improve outcomes for this community."

"As a mom to a young boy living with Alexander disease and an advocate for this community, I have seen firsthand the profound impact this disease has on individuals and their families. Today's approval represents a fundamental shift, changing the conversation from 'How do we manage this disease' to 'How can we treat it,'" said Emily Petty, president, End Alexander Disease. "For far too long, receiving a diagnosis of Alexander disease was accompanied by uncertainty and the difficult reality that there were no available treatments. Today, that begins to change. ZANVASTRO marks a defining moment and brings a new sense of possibility to our community."

The FDA approval was based on positive results from the pivotal study of ZANVASTRO in people living with AxD. The pivotal study met its primary endpoint in individuals ≥ 5 years of age, with ZANVASTRO 50 mg demonstrating statistically significant and clinically meaningful stabilization of gait speed as assessed by the 10-Meter Walk Test (10MWT), a commonly used measure of gross motor function in neurologic disease, compared to control at Week 61 (least square mean difference 33.3%, p=0.041). ZANVASTRO also demonstrated improvement in gross motor function in patients 2 to 4 years of age as assessed by the Gross Motor Function Measure-88 (GMFM-88), a well-established motor endpoint, compared to control at Week 61. Secondary and exploratory endpoint results from patient/caregiver- and clinician-reported outcome assessments consistently favored ZANVASTRO.

ZANVASTRO demonstrated a favorable safety and tolerability profile, with most adverse events (AEs) being mild or moderate in severity. Serious treatment-emergent adverse events (TEAEs) occurred less frequently in the ZANVASTRO group compared to control.

Ionis is committed to helping people access the medicines they are prescribed and will offer a full suite of services for people prescribed ZANVASTRO through Ionis Every Step™. As part of Ionis Every Step, patients will have access to a wide range of support and resources including disease state and product education for patients and caregivers, access to a dedicated Patient Education Manager, assistance with the insurance approval process, information on affordability programs and other ongoing services and resources throughout the treatment journey. Visit ZANVASTRO.com for more information.

With the approval of ZANVASTRO, the FDA granted Ionis a Rare Pediatric Disease Priority Review Voucher (PRV), a program designed to incentivize the development of therapies for serious and life-threatening diseases by providing a mechanism to potentially accelerate regulatory review timelines for subsequent applications.

ZANVASTRO will be available in the U.S. in the coming weeks.

In June 2026, Ionis entered into a license agreement with Recordati, a global pharmaceutical company headquartered in Italy, focused on specialty and rare diseases, under which Recordati obtained exclusive rights to develop and commercialize zilganersen in all countries outside the U.S. Ionis is working closely with Recordati on preparing regulatory submissions in Europe and Japan, which are expected in 2027.

Webcast

Ionis will hold a webcast on Friday, Sept. 4 at 10:00 a.m. ET to discuss the FDA approval. Interested parties may access the webcast here. A webcast replay will be available for a limited time.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS
Aseptic Meningitis

If symptoms consistent with aseptic meningitis develop, diagnostic workup and treatment should be initiated according to the standard of care.

Adverse reactions of aseptic meningitis (also called chemical meningitis or drug-induced aseptic meningitis) were reported in patients treated with ZANVASTRO during the double-blind and open-label periods of Study 1. One patient experienced a serious adverse reaction of aseptic meningitis during the double-blind treatment period of Study 1, which reoccurred in the open-label extension period and required dose interruption and pretreatment with intravenous dexamethasone prior to subsequent administration of ZANVASTRO. Despite corticosteroid premedication, CSF white blood cell (WBC) and protein increased with continued exposure, but the patient remained asymptomatic and did not require discontinuation from treatment. In addition, nonserious adverse drug reactions of CSF WBC increases have also been reported with ZANVASTRO.

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥25% patients treated with ZANVASTRO and greater than control) were vomiting, back pain, cough, headache, and post-lumbar puncture syndrome.

Patients Less Than 2 Years of Age
The adverse reactions of patients less than 2 years of age are expected to be similar to that of pediatric patients 2 years of age and older.

Please see full Prescribing Information for ZANVASTRO.

About the ZANVASTRO 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 ZANVASTRO 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 week 60, eligible participants entered a 60-week open-label treatment period, followed by a 120-week open-label long-term extension period. During the long-term extension, participants in the 25 mg dose cohort transitioned to the 50 mg dose cohort. Participants in countries where zilganersen has not been or is not commercially available can continue to receive zilganersen treatment through a 240-week extended long-term extension period, which includes 20 additional doses, followed by a 28-week post-treatment follow-up period. The primary endpoint was 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 Alexander Disease (AxD)

AxD is an ultra-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 including support of neurons and oligodendrocytes, which maintain the myelin sheath around 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.

About ZANVASTRO™ (zilganersen)

ZANVASTRO™ (zilganersen) is approved by the U.S. Food and Drug Administration (FDA) for the treatment of Alexander disease (AxD) in pediatric and adult patients. ZANVASTRO is an RNA-targeted therapy designed to inhibit production of excess glial fibrillary acidic protein (GFAP) that accumulates as a result of pathogenic variants in the *GFAP* gene. For more information about ZANVASTRO, visit ZANVASTRO.com.

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 12 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 ZANVASTRO, Ionis' technologies and other products in development 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 Pharmaceuticals and its subsidiaries.

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