Olezarsen sNDA accepted by the FDA for Priority Review for the treatment of severe hypertriglyceridemia (sHTG)

February 26, 2026

– PDUFA date set for June 30, 2026 –

CARLSBAD, Calif.--(BUSINESS WIRE)--Feb. 26, 2026-- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today announced that the U.S. Food and Drug Administration (FDA) has accepted for Priority Review the supplemental New Drug Application (sNDA) for olezarsen for severe hypertriglyceridemia (sHTG). The FDA has set a Prescription Drug User Fee Act (PDUFA) target action date of June 30, 2026.

"Current standard of care therapies for sHTG provide limited benefit, leaving people vulnerable to recurrent and debilitating acute pancreatitis attacks with serious, long-term health consequences," said Brett P. Monia, Ph.D., chief executive officer, Ionis. "The FDA's Priority Review designation underscores the urgent need for additional treatment options and will enable us to bring olezarsen to patients as quickly as possible. This milestone represents a significant step toward our goal of delivering the first-ever treatment shown to reduce the risk of potentially life-threatening acute pancreatitis attacks in people with sHTG."

The sNDA and Priority Review designation were based on the positive results from the Phase 3 CORE and CORE2 studies of olezarsen. In the studies, olezarsen demonstrated a highly statistically significant placebo-adjusted reduction in triglyceride levels of up to 72% and an 85% reduction in acute pancreatitis events with favorable safety and tolerability. Additionally, nearly 90% of olezarsen-treated patients achieved triglyceride levels less than 500 mg/dL, which is below the risk threshold for acute pancreatitis. The data were published in *The New England Journal of Medicine* and presented at the American Heart Association Scientific Sessions.

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 U.S. FDA previously granted olezarsen Breakthrough Therapy designation in November 2025.

About the CORE and CORE2 Studies

CORE (NCT05079919; n=617) and CORE2 (NCT05552326; n=446), conducted with The TIMI Study Group, are Phase 3 global, multicenter, randomized, double-blind, placebo-controlled trials investigating the safety and efficacy of olezarsen for severe hypertriglyceridemia (sHTG). Participants aged 18 and older with triglyceride levels ≥500 mg/dL were enrolled. Participants were required to be on standard of care therapies for elevated triglycerides. At baseline, 47% and 37% of participants had fasting triglycerides ≥880 mg/dL in CORE and CORE2, respectively. Participants were randomized to receive 50 mg or 80 mg of olezarsen or placebo every 4 weeks via subcutaneous injection for 12 months. The primary endpoint was the percent change from baseline in fasting triglycerides at six months compared to placebo.

About Severe Hypertriglyceridemia

Severe hypertriglyceridemia (sHTG) is defined by very high triglycerides (≥500 mg/dL) and characterized by an increased risk of acute pancreatitis and other serious health complications. Considered a medical emergency, acute pancreatitis causes debilitating abdominal pain that often requires prolonged hospitalization, can lead to permanent organ damage and can become life-threatening. Preventing the first attack is key. In people with a history of acute pancreatitis episodes, the risk of future attacks is even greater. Current standard of care therapies for sHTG and lifestyle modifications (such as diet and exercise) do not sufficiently or consistently lower triglyceride levels or reduce the risks of sHTG in all patients. Approximately 3 million people are living with sHTG in the U.S., including more than 1 million who are considered high risk. High-risk sHTG includes those with triglycerides ≥880 mg/dL or triglycerides ≥500 mg/dL and a history of acute pancreatitis or other comorbidities.

About Olezarsen

Olezarsen is an investigational RNA-targeted medicine being evaluated for the treatment of sHTG. Olezarsen is designed to lower the body's production of apoC-III, a protein produced in the liver that regulates triglyceride metabolism in the blood. Olezarsen is approved in the U.S. and the European Union as TRYNGOLZA® for adults with familial chylomicronemia syndrome (FCS).

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, the therapeutic and commercial potential of our commercial medicines, olezarsen, 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, 2024, 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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