TRYNGOLZA™ (olezarsen) approved in the EU for severe hypertriglyceridemia (sHTG)

November 17, 2026

– TRYNGOLZA is now the first and only RNA-targeted therapy indicated in the EU for sHTG ≥880 mg/dL (≥10 mmol/L) –

– Approximately 700,000 people in the EU5 are estimated to have triglyceride levels ≥880 mg/dL (≥10 mmol/L) and at high risk of developing acute pancreatitis –

CARLSBAD, Calif.--(BUSINESS WIRE)--Nov. 17, 2026-- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today announced that the European Commission (EC) has approved TRYNGOLZA™ (olezarsen) as an adjunct to diet, in combination with other lipid-lowering therapies, for the treatment of adult patients with severe hypertriglyceridemia (sHTG, fasting triglyceride levels of ≥880 mg/dL [≥10 mmol/L]). TRYNGOLZA is the first and only RNA-targeted therapy authorized in the EU for adults with sHTG ≥880 mg/dL (≥10 mmol/L). The approval follows an early positive opinion from the Committee for Medicinal Products for Human Use (CHMP) in October and expands the marketing authorization for TRYNGOLZA, which is already indicated for familial chylomicronemia syndrome (FCS), into a broader patient population.

The EU approval is based on results from the pivotal Phase 3 CORE and CORE2 studies in adult patients with sHTG and triglyceride levels ≥880 mg/dL (≥10 mmol/L). These studies met their primary endpoint, with TRYNGOLZA demonstrating a statistically significant placebo-adjusted mean reduction in fasting triglyceride levels and reduction in acute pancreatitis events. TRYNGOLZA demonstrated a favorable safety and tolerability profile. The data were published in *The New England Journal of Medicine.*

“This approval is based on the robust clinical evidence supporting the compelling profile of TRYNGOLZA for sHTG and an example of the broad impact of Ionis’ science,” said Brett P. Monia, Ph.D., chief executive officer, Ionis. “We are proud to work with our long-standing partner Sobi to bring TRYNGOLZA to people in need across the EU."

“Acute pancreatitis is a potentially life-threatening medical emergency that may require intensive care admission and prolonged hospitalization,” said Erik S.G. Stroes, MD, PhD, professor of vascular medicine, Amsterdam UMC. “Some patients experience permanent organ damage and lasting effects on their quality of life. There is an unmet need for patients with sHTG for new, effective therapies to help reduce the risk of acute pancreatitis.”

“The European Commission’s approval of TRYNGOLZA for the treatment of sHTG is an important step forward for patients in Europe who remain at increased risk of acute pancreatitis despite diet and existing lipid-lowering therapies,” said Lydia Abad-Franch, MD, head of R&D and medical affairs and chief medical officer, Sobi. “The EU decision marks meaningful progress for eligible patients living with sHTG.”

TRYNGOLZA was discovered, developed and is commercialized in the U.S. by Ionis Pharmaceuticals. The U.S. Food and Drug Administration approved TRYNGOLZA in June as an adjunct to diet to reduce triglycerides and the risk of acute pancreatitis in adults with sHTG (triglycerides ≥500 mg/dL). Sobi and Ionis entered into a license agreement under which Sobi has exclusive rights to commercialize TRYNGOLZA in ex-U.S. geographies except Canada and China.

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 (≥5.65 mmol/L) were enrolled. Participants were required to be on standard of care therapies for elevated triglycerides. At baseline, 43% of participants had fasting triglycerides ≥880 mg/dL (≥10 mmol/L). Participants were randomized to receive 50 mg or 80 mg of olezarsen or placebo every four weeks via subcutaneous injection for 12 months. The primary endpoint was the percentage change from baseline in fasting triglycerides at six months compared to placebo.

About Severe Hypertriglyceridemia

Severe hypertriglyceridemia (sHTG) is defined by severely high triglyceride levels ≥500 mg/dL (≥5.65 mmol/L), and triglyceride levels ≥880 mg/dL (≥10 mmol/L) are often associated with the increased accumulation of chylomicrons in the blood and with an increased risk of acute pancreatitis and other morbidities. 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. Approximately two million people are living with sHTG in the EU5, including approximately 700,000 with TG levels ≥880 mg/dL (≥10 mmol/L).

About TRYNGOLZA™ (olezarsen)

TRYNGOLZA™ (olezarsen) is an RNA-targeted therapy designed to lower the body's production of apoC-III, a protein produced in the liver that regulates triglyceride metabolism in the blood. TRYNGOLZA is approved in the U.S. and EU as an adjunct to diet to reduce triglycerides (TG) and the risk of acute pancreatitis in adults with severe hypertriglyceridemia (sHTG). TRYNGOLZA is also approved in the U.S., EU and other countries for adults with familial chylomicronemia syndrome (FCS), a rare form of sHTG. Visit TRYNGOLZA.com for more information.

INDICATIONS

Familial Chylomicronemia Syndrome (FCS)

TRYNGOLZA (olezarsen) is indicated as an adjunct to diet to reduce triglycerides (TG) in adults with familial chylomicronemia syndrome (FCS).

Severe Hypertriglyceridemia (sHTG)

TRYNGOLZA is indicated as an adjunct to diet to reduce TG and the risk of acute pancreatitis in adults with severe hypertriglyceridemia (sHTG: TG ≥500 mg/dL).

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

TRYNGOLZA is contraindicated in patients with a history of serious hypersensitivity to TRYNGOLZA or any of the excipients in TRYNGOLZA. Hypersensitivity reactions requiring medical treatment have occurred.

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

Hypersensitivity reactions (including symptoms of bronchospasm, diffuse erythema, facial swelling, urticaria, chills, and myalgias) have been reported in patients treated with TRYNGOLZA. Advise patients on the signs and symptoms of hypersensitivity reactions and instruct patients to promptly seek medical attention and discontinue use of TRYNGOLZA if hypersensitivity reactions occur.

Liver Enzyme Abnormalities

TRYNGOLZA can cause increases in liver enzymes and hepatic fat in adults. Increases in liver enzymes were more frequently reported with the 80 mg dose as compared with the 50 mg dose. Consider liver enzyme testing before TRYNGOLZA initiation or an increase in dosage and when clinically indicated thereafter. If persistent elevations in liver enzymes occur, consider dose interruption and/or dose reduction. If serious hepatic injury with clinical symptoms and/or hyperbilirubinemia or jaundice occurs, promptly discontinue TRYNGOLZA.

ADVERSE REACTIONS

Adverse Reactions for FCS

Most common adverse reactions in patients with FCS (incidence >5% of TRYNGOLZA-treated patients and >3% higher frequency than placebo) were injection site reactions, decreased platelet count, and arthralgia.

Adverse Reactions for sHTG

Most common adverse reactions in patients with sHTG (incidence ≥2% higher than placebo) were injection site reactions and liver enzyme increases.

Please see U.S. Prescribing Information for TRYNGOLZA. Please see Important Safety Information throughout and full Prescribing Information for TRYNGOLZA.

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 TRYNGOLZA, Ionis' technologies and other products in development. 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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