TRYNGOLZA® (olezarsen) approved by the FDA as the first and only treatment to reduce triglycerides and the risk of acute pancreatitis in patients with severe hypertriglyceridemia (sHTG)

June 24, 2026

– Proven to deliver significant and robust triglyceride reductions –

– Only treatment for sHTG indicated to reduce the risk of acute pancreatitis –

– Ionis' first independent commercial launch in a prevalent condition –

– Ionis to host webcast today at 3:30 p.m. ET –

CARLSBAD, Calif.--(BUSINESS WIRE)--Jun. 24, 2026-- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today announced that the U.S. Food and Drug Administration (FDA) has approved TRYNGOLZA® (olezarsen) as an adjunct to diet to reduce triglycerides (TG) and the risk of acute pancreatitis in adults with severe hypertriglyceridemia (sHTG: TG greater than or equal to 500 mg/dL). TRYNGOLZA is available in a 50 mg or 80 mg dose and is self-administered once monthly via an autoinjector. sHTG is characterized by an increased risk of acute pancreatitis, which causes debilitating abdominal pain that often leads to repeated and prolonged hospitalization, permanent organ damage and can be life-threatening.

This press release features multimedia. View the full release here: https://www.businesswire.com/news/home/20260624119051/en/

"The approval of TRYNGOLZA marks an historic advance for people who have long struggled to control their dangerously high triglycerides, providing the only approved therapy for sHTG to dramatically lower triglyceride levels and significantly reduce acute pancreatitis events," said Brett P. Monia, Ph.D., chief executive officer, Ionis. "TRYNGOLZA reflects the strength of Ionis' innovative science and our commitment to transforming patients' lives. As our first independent launch in a prevalent disease, this milestone builds on our success in familial chylomicronemia syndrome, a rare form of sHTG, and marks a defining moment for Ionis as we bring our groundbreaking medicines to even more patients in need. We are deeply grateful to the clinical trial participants, investigators, the Ionis team and many others whose dedication made this achievement possible."

"As a physician, I have seen firsthand how challenging it can be for patients with sHTG to lower their triglycerides below 500 mg/dL, despite background lipid-lowering therapies and lifestyle changes, which leaves them at risk of a devastating and potentially life-threatening acute

TRYNGOLZA (olezarsen) product image

pancreatitis attack," said Archna Bajaj, M.D., assistant professor of clinical medicine, University of Pennsylvania. "TRYNGOLZA is a transformational new therapy that showed unprecedented, clinically meaningful outcomes for sHTG, with the potential to redefine the treatment paradigm."

The FDA approval was based on positive results from the Phase 3 CORE and CORE2 studies, which were published in *The New England Journal of Medicine*.

In the CORE and CORE2 studies, TRYNGOLZA demonstrated rapid and consistent triglyceride control, lowering fasting triglyceride levels by up to 72% compared to placebo at six months and sustaining those reductions at 12 months. Additionally, TRYNGOLZA significantly reduced acute pancreatitis events by up to 91%. Among patients treated with TRYNGOLZA with baseline and 12-month data, 86% achieved triglyceride levels below 500 mg/dL, a critical threshold for reducing acute pancreatitis risk. The number needed to treat (NNT) over one year to prevent one episode of acute pancreatitis was 20 in the overall cohort and four in patients with triglycerides ≥880 mg/dL and a prior history of acute pancreatitis, indicating a strong clinical benefit across the spectrum of sHTG patients and an exceptional clinical benefit in the highest risk subgroup.[1]

Across the clinical program, TRYNGOLZA demonstrated a favorable safety and tolerability profile. The most common adverse reactions in patients with sHTG (incidence ≥2% higher than placebo) were injection site reactions and liver enzyme increases.

"With limited options to lower triglycerides, people living with sHTG often face a constant and real fear that a debilitating acute pancreatitis attack could strike at any time without warning," said Emily Draud, interim executive director, National Pancreas Foundation. "The availability of TRYNGOLZA for sHTG represents an important new option for this community, offering hope for people who have been waiting for a new treatment to reduce the risk of acute pancreatitis by significantly lowering their triglyceride levels. It also underscores the urgent need for continued innovation and improved care for patients living with this serious condition."

Ionis is committed to helping people access the medicines they are prescribed and will offer a full suite of services for people prescribed TRYNGOLZA through Ionis Every Step™. Ionis Every Step offers personal support, including nutrition information and injection training, insurance support and financial assistance programs. Visit TRYNGOLZA.com for more information.

TRYNGOLZA will be available for sHTG in the U.S. in July.

Webcast

Ionis will hold a webcast today at 3:30 p.m. ET to discuss the FDA approval. Interested parties may access the webcast here. A webcast replay will be available for a limited time.

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

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 four weeks via subcutaneous injection for 12 months.

The CORE and CORE2 studies met the primary endpoint, with both 50 mg and 80 mg monthly TRYNGOLZA doses. TRYNGOLZA demonstrated a statistically significant reduction in fasting triglycerides of 49%-63% (50 mg) and 55%-72% (80 mg) compared to placebo at six months. Additionally, TRYNGOLZA demonstrated a statistically significant 91% (50 mg) and 76% (80 mg) reduction in acute pancreatitis events at 12 months, with a pooled reduction of 85%.

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. More than 3 million people are living with sHTG in the U.S., including approximately 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 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 United States as an adjunct to diet to reduce triglycerides (TG) and the risk of acute pancreatitis in adults with severe hypertriglyceridemia (sHTG: TG greater than or equal to 500 mg/dL). TRYNGOLZA is also approved in the United States, European Union and other countries for adults with familial chylomicronemia syndrome (FCS), a rare form of sHTG. Visit TRYNGOLZA.com for more information.

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 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.

[1] What are poor, acceptable, and great Number Needed to Treat (NNT) figures? Dr. Oracle. AI. Updated December 13, 2025. Accessed May 8, 2026. https://www.droracle.ai/articles/612269/what-are-poor-acceptable-and-great-number-needed-to

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