SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(d) OF THE
SECURITIES EXCHANGE ACT OF 1934

Date of report (Date of earliest event reported): December 19, 2024

IONIS PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware
(State or Other Jurisdiction of Incorporation)

000-19125	**33-0336973**
(Commission File No.)	(IRS Employer Identification No.)

2855 Gazelle Court
Carlsbad, CA 92010
(Address of Principal Executive Offices and Zip Code)

Registrant's telephone number, including area code: **(760) 931-9200**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol	Name of each exchange on which registered
Common Stock, $.001 Par Value	"IONS"	The Nasdaq Stock Market, LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (Section 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (Section 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 Other Events.

On December 19, 2024, Ionis Pharmaceuticals, Inc. issued a press release announcing that the U.S. Food and Drug Administration has approved Tryngolza™ (olezarsen) as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome.

A copy of this press release is attached as Exhibit 99.1 to this Current Report and incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press Release dated December 19, 2024.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

IONIS PHARMACEUTICALS, INC.

Dated: December 20, 2024

By: /s/ Patrick R. O'Neil

PATRICK R. O'NEIL
Executive Vice President, Chief Legal Officer and General Counsel

TRYNGOLZA™ (olezarsen) approved in U.S. as first-ever treatment for adults living with familial chylomicronemia syndrome as an adjunct to diet

- *TRYNGOLZA shown to significantly reduce triglycerides and substantially reduce acute pancreatitis events in adults with FCS; a rare, highly debilitating and life-threatening disease*
- *Indicated for adults with FCS regardless of genetically or clinically confirmed diagnosis*
- *TRYNGOLZA is the first of four independent launches planned over the next three years, pending approvals*
- *Ionis to host webcast today at 6:45 pm ET*

CARLSBAD, Calif., December 19, 2024 -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) announced today that the U.S. Food and Drug Administration (FDA) has approved TRYNGOLZA™ (olezarsen) as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS), a rare, genetic form of severe hypertriglyceridemia (sHTG) that can lead to potentially life-threatening acute pancreatitis (AP). TRYNGOLZA is the first-ever FDA-approved treatment that significantly and substantially reduces triglyceride levels in adults with FCS and provides clinically meaningful reduction in AP events when used with an appropriate diet (≤20 grams of fat per day). TRYNGOLZA is self-administered via an auto-injector once monthly.

“Today’s FDA approval of TRYNGOLZA heralds the arrival of the first-ever FCS treatment in the U.S. – a transformational moment for patients and their families. For the first time, adults with FCS can now access a treatment that substantially reduces triglycerides and the risk of debilitating and potentially life-threatening acute pancreatitis,” said Brett P. Monia, Ph.D., chief executive officer, Ionis. “We are proud of our long-standing partnership with the FCS community and are grateful to the patients, families and investigators who participated in our clinical studies, enabling Ionis to make this new treatment a reality. The FDA approval of TRYNGOLZA is also a pivotal moment for Ionis, representing our evolution into a fully integrated commercial-stage biotechnology company – a goal we set out to achieve five years ago. With our rich pipeline of potentially life-changing medicines, we expect TRYNGOLZA to be the first in a steady cadence of innovative medicines we will deliver independently to people living with serious diseases.”

The FDA approval was based on positive data from the global, multicenter, randomized, placebo-controlled, double-blind Phase 3 Balance clinical trial in adult patients with genetically identified FCS and fasting triglyceride levels ≥880 mg/dL. In the Balance study, TRYNGOLZA 80 mg demonstrated a statistically significant placebo-adjusted mean reduction in triglyceride levels of 42.5% from baseline to six months (p=0.0084). Reductions from baseline to 12 months were further improved, with TRYNGOLZA achieving a placebo-adjusted 57% mean reduction in triglycerides. TRYNGOLZA also demonstrated a substantial, clinically meaningful reduction in AP events over 12 months; one patient (5%) experienced one episode of AP in the TRYNGOLZA group compared with seven patients (30%) who experienced 11 total episodes of AP in the placebo group.

TRYNGOLZA demonstrated a favorable safety profile. The most common adverse reactions (incidence >5% of TRYNGOLZA-treated patients and at a >3% higher frequency than placebo) were injection site reactions (19% and 9%, respectively), decreased platelet count (12% and 4%, respectively) and arthralgia (9% and 0%, respectively).

Results from the Phase 3 Balance study were previously published in *The New England Journal of Medicine (NEJM)*.

“With no treatment options previously available, we were limited to relying only on extremely strict diet and lifestyle changes as the sole preventative treatment option,” said Alan Brown, M.D., FNLA, FACC, FAHA, clinical professor of medicine, Rosalind Franklin University of Medicine and Science; Balance trial investigator. “The FDA approval of TRYNGOLZA is an important moment for people living with FCS, their families and physicians who now, for the first time, have a treatment that significantly lowers triglycerides and decreases the risk of potentially life-threatening acute pancreatitis events, as an adjunct to a low-fat diet. I am excited to have a medicine I can prescribe to my patients that has been shown to change the course of their disease.”

FCS is a rare, genetic, potentially life-threatening form of sHTG that prevents the body from breaking down fats and severely impairs the body's ability to remove triglycerides from the bloodstream due to an impaired function of the enzyme lipoprotein lipase (LPL). While healthy levels for adults are below 150 mg/dL, people with FCS often have triglyceride levels of more than 880 mg/dL and often have a history of pancreatitis. Those living with FCS have a high risk of potentially fatal AP, which is a painful inflammation of the pancreas, and chronic health issues such as fatigue and severe, recurrent abdominal pain. People living with FCS can also experience psychological and financial stress, which can significantly impact their quality of life. In the U.S., FCS is estimated to impact up to approximately 3,000 people, the vast majority of whom remain undiagnosed.

"As a rare and difficult to diagnose disease, FCS has a profound impact on the lives of patients and families. Many people living with FCS have experienced severe pain their whole lives – sometimes so intense they require lengthy hospitalization stays – and struggle through life with daily fatigue, nausea, brain fog and stomach pain," said Lindsey Sutton Bryan, co-founder and co-president, FCS Foundation. "Until now, our treatment options have been limited, relying on diet alone to try to manage triglyceride levels and keep acute pancreatitis attacks at bay. For the first time, adults with FCS have seen their hope for a treatment become a reality."

TRYNGOLZA will be available in the U.S. before year end.

Ionis is committed to helping people access the medicines they are prescribed and will offer a suite of services designed to meet the unique needs of the FCS community through Ionis Every Step™. As part of Ionis Every Step, patients and healthcare providers will have access to services throughout the treatment journey provided by dedicated Patient Education Managers and Ionis Every Step Case Managers, including insurance and affordability support, as well as services and resources, such as disease and nutrition education. Visit TRYNGOLZA.com for more information.

TRYNGOLZA was reviewed by the FDA under Priority Review and had previously been granted Fast Track designation for the treatment of FCS, Orphan Drug designation and Breakthrough Therapy designation. Olezarsen is undergoing review in the European Union and regulatory filings in other countries are planned. Olezarsen is currently being evaluated in three Phase 3 clinical trials – CORE, CORE2 and ESSENCE – for the treatment of sHTG. Olezarsen has not been reviewed or approved for the treatment of sHTG by regulatory authorities.

Webcast
Ionis will hold a webcast today at 6:45 pm ET to discuss the FDA approval. Interested parties may access the webcast here. A webcast replay will be available for a limited time.

About TRYNGOLZA™ (olezarsen)
TRYNGOLZA™ (olezarsen) was approved by the U.S. Food and Drug Administration as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS). TRYNGOLZA is an RNA-targeted medicine designed to lower the body's production of apoC-III, a protein produced in the liver that is a key regulator of triglyceride metabolism. It is the only treatment currently indicated in the U.S. for FCS, a potentially life-threatening disease. For more information about TRYNGOLZA, visit TRYNGOLZA.com.

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.

ADVERSE REACTIONS

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

Please see full Prescribing Information for TRYNGOLZA.

About Familial Chylomicronemia Syndrome (FCS)

FCS is a rare, genetic disease characterized by extremely elevated triglyceride levels. It is caused by impaired function of the enzyme lipoprotein lipase (LPL). Because of limited LPL production or function, people with FCS cannot effectively break down chylomicrons, lipoprotein particles that are 90% triglycerides. FCS is estimated to impact up to approximately 3,000 people in the U.S. People living with FCS are at high risk of acute pancreatitis (AP) in addition to other chronic health issues such as fatigue and severe, recurrent abdominal pain. People living with FCS are sometimes unable to work, adding to the burden of disease.

About the Balance Study

Balance is a global, multicenter, randomized, double-blind, placebo-controlled Phase 3 study evaluating the efficacy and safety of olezarsen in patients with FCS at six and 12 months. The primary endpoint was the percent change from baseline in fasting triglyceride levels at six months compared to placebo. Secondary endpoints included percent changes in triglyceride levels at 12 months, percent changes in other lipid parameters and adjudicated acute pancreatitis event rates over the treatment period. Following treatment and the end-of-trial assessments, patients were eligible to enter an open-label extension study to continue receiving olezarsen once every four weeks.

About Ionis Pharmaceuticals, Inc.

For three decades, Ionis has invented medicines that bring better futures to people with serious diseases. Ionis has discovered and developed six marketed medicines for serious diseases, including breakthrough medicines for neurologic and cardiovascular diseases. Ionis has a leading pipeline in neurology, cardiology and other 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 but not limited to those related to our commercial products and the medicines in our pipeline, and particularly 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 Dec. 31, 2023, and most recent Form 10-Q, which are on file with the SEC. Copies of these and other documents are available at www.Ionis.com.

Ionis Pharmaceuticals® and TRYNGOLZA™ are trademarks of Ionis Pharmaceuticals, Inc.

Ionis Investor Contact:
D. Wade Walke, Ph.D.
info@ionis.com 760-603-2331

Ionis Media Contact:
Hayley Soffer
media@ionis.com 760-603-4679

###