



Ionis presents positive results from Phase 3 Balance study of olezarsen for familial chylomicronemia syndrome

April 7, 2024

- *Olezarsen met the primary endpoint with statistically significant reduction of fasting triglycerides and showed substantial, clinically meaningful reduction in acute pancreatitis events –*
- *Results demonstrate olezarsen may represent a novel treatment option for this rare, life-threatening disease, for which there are no approved treatments in the U.S. –*
- *Data presented today at ACC 2024 and published in The New England Journal of Medicine –*
- *Ionis to host webcast on Monday, April 8 at 10:00 am ET –*

CARLSBAD, Calif., April 7, 2024 /PRNewswire/ -- [Ionis Pharmaceuticals, Inc.](#) (Nasdaq: IONS) today announced full results from the Phase 3 Balance study of Ionis' lead independent investigational medicine, olezarsen, for the treatment of adults with familial chylomicronemia syndrome (FCS). The olezarsen 80 mg monthly dose met the primary endpoint of significantly reducing triglycerides (TGs) in patients with genetically validated FCS at six months. In addition, olezarsen demonstrated robust and sustained reductions in TGs and serum apolipoprotein C-III (apoC-III) levels. Importantly, olezarsen reduced the incidence of acute pancreatitis (AP) events over the 12-month treatment period compared to placebo. Olezarsen also demonstrated a favorable safety and tolerability profile. These results were presented in an oral presentation at the 2024 American College of Cardiology (ACC) Annual Meeting in Atlanta, Georgia and published simultaneously in [The New England Journal of Medicine \(NEJM\)](#). Based on these data, Ionis is pursuing regulatory approval of olezarsen as a potential breakthrough treatment for adults with FCS.

"As a physician who has seen first-hand the struggles of people living with FCS and its serious complications, there is significant need for an effective therapy to lower triglycerides and reduce acute pancreatitis events," said Erik Stroes, M.D., professor of medicine, Amsterdam University Medical Centers, and a principal investigator of the Balance study. "Olezarsen represents a potentially life-changing new medicine for these patients who experience debilitating chronic symptoms, including abdominal pain and cognitive symptoms, as well as hospitalizations associated with potentially fatal acute pancreatitis events."

Balance Study Results

In the study, patients were treated with olezarsen 80 mg (n=22), 50 mg (n=21) or placebo (n=23) once every four weeks.

- In the 80 mg group, olezarsen met the primary endpoint, with a statistically significant placebo-adjusted reduction in TG levels from baseline to six months (44%, $p < 0.001$).
 - Reductions from six to 12 months were sustained, with olezarsen 80 mg achieving a placebo-adjusted 59% reduction in TGs.
 - ApoC-III placebo-adjusted reductions were robust and sustained at six and 12 months (74% and 81% reductions, respectively).
- In the 50 mg group, olezarsen reduced TG levels, however this difference was not statistically significant at six months compared to placebo (22%, $p = 0.078$).
 - Reductions from six to 12 months were improved, with olezarsen 50 mg achieving a placebo-adjusted 44% reduction in TGs.
- Olezarsen-treated patients had markedly fewer AP events during the 12-month period, compared to placebo.
 - Eleven episodes of AP occurred in the placebo group versus one episode in the 80 mg olezarsen group and one episode in the 50 mg group.
 - Furthermore, there was a substantially greater time to the first event with olezarsen compared to placebo (one year (80 mg) and 102 days (50 mg), vs. nine days for placebo).
- Olezarsen-treated patients experienced a placebo-adjusted 84% reduction in all-cause hospitalizations between baseline and 12 months.
- A favorable safety and tolerability profile was observed, with a higher number of treatment-emergent adverse events (TEAEs) in the placebo group. There were no serious TEAEs related to olezarsen.
 - The most common AEs were COVID-19, abdominal pain and diarrhea, none of which were more frequent in patients treated with either dose of olezarsen versus placebo.
 - Serious AEs occurred in 14% of patients treated with olezarsen 80 mg, 19% treated with olezarsen 50 mg, and 39% treated with placebo.

"Balance is the first clinical study to validate the association of reduced triglyceride levels with reduced incidence of acute pancreatitis events in patients with severely elevated triglycerides. This important finding supports the potential for olezarsen to be the standard of care for patients with FCS, if approved. These data further strengthen our confidence for a successful outcome in the ongoing Phase 3 CORE studies evaluating olezarsen in the much more prevalent severe hypertriglyceridemia patient population," said Brett P. Monia, Ph.D., chief executive officer of Ionis. "Our team looks forward to working closely with the FDA to advance the first potential treatment for FCS in the U.S., and to successfully delivering Ionis' first independent commercial launch later this year, assuming priority review. We offer our sincerest gratitude to the patients and investigators who participated in this pivotal study."

The ACC Balance presentation can be found on [Ionis' website](#) after today's presentation at 10:08 am ET.

In addition to the Balance data, a late-breaking abstract entitled, "Efficacy and Safety of Olezarsen in Patients with Hypertriglyceridemia and High Cardiovascular Risk: Primary Results of the Bridge-TIMI 73a Trial" was also presented at ACC and published in [NEJM](#).

Webcast

Ionis will host a webcast to discuss the detailed results from the Balance study on Monday, April 8 at 10:00 am ET. Interested parties may access the webcast [here](#). A webcast replay will be available for a limited time.

About the Balance Study

The global, multicenter, randomized, double-blind, placebo-controlled Phase 3 Balance study ([NCT04568434](#)) enrolled 66 patients aged 18 and older with confirmed FCS. Patients in the study received background therapies including statins, fibrates and omega-3 fatty acids. Patients were randomized in a 1:1:1 ratio to receive olezarsen 80 mg or 50 mg or placebo via subcutaneous injection once every four weeks for 53 weeks. 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.

About Olezarsen

Olezarsen is an RNA-targeted investigational **Ligand Conjugated Antisense** (LICA) medicine being evaluated for people at risk of disease due to elevated triglyceride levels, including those with familial chylomicronemia syndrome (FCS). Olezarsen is designed to inhibit the body's production of apoC-III, a protein produced in the liver that regulates triglyceride metabolism in the blood.^{1,2} The U.S. FDA granted [olezarsen Fast Track designation](#) for the treatment of FCS in January 2023, as well as [Orphan Drug designation](#) and [Breakthrough Therapy designation](#) in February 2024. In addition to FCS, Ionis is evaluating olezarsen for the treatment of severe hypertriglyceridemia (sHTG) in Phase 3 clinical trials.

Olezarsen is an investigational medicine that has not been reviewed or approved for the treatment of any disease by any regulatory authority.

About 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).³ Because of limited LPL production or function, people with FCS cannot effectively break down chylomicrons, lipoprotein particles that are 90% triglycerides.^{3,4} FCS is estimated to impact one to 13 people per million in the U.S.^{5,6,7} 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.^{3,8,9} People living with FCS are sometimes unable to work, adding to the burden of disease.⁹

Currently, there are no U.S. FDA-approved therapies for the treatment of FCS and standard triglyceride lowering therapies are generally ineffective in patients with FCS.^{10,11} People living with this condition currently rely solely on nutrition management through extremely restrictive and difficult to manage diets to navigate the health risks associated with FCS.^{11,12}

About Ionis Pharmaceuticals, Inc.

For three decades, Ionis has invented medicines that bring better futures to people with serious diseases. Ionis currently has five marketed medicines and 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 [ionispharma.com](#) and follow us on X (Twitter) and LinkedIn.

Forward-looking Statements

This press release includes forward-looking statements regarding olezarsen, Ionis' business, and the therapeutic and commercial potential of Ionis' commercial medicines, additional medicines in development and technologies. 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.ionispharma.com](#).

Ionis Pharmaceuticals® is a registered trademark of Ionis Pharmaceuticals, Inc.

Ionis Pharmaceuticals Investor Contact: D. Wade Walke, Ph.D. - info@ionisph.com - 760-603-2331; Ionis Pharmaceuticals Media Contact: Hayley

Soffer - CorporateCommunications@ionisph.com - 760-603-4679

¹Alexander VJ, et al. Eur Heart J 2019;40(33):2785-2796.

²Tardif JC, et al. Eur Heart J 2022;43(14):1401-1412.

³Gaudet D, et al. N Engl J Med. 2014;371:2200-2206.

⁴Ginsberg HN, et al. Eur Heart J. 2021;42:4791-4806.

⁵Pallazola VA, et al. Eur J Prev Cardiol 2020;27(19):2276-8.

⁶Warden BA, et al. J Clin Lipidol 2020;14(2):201-6.

⁷Tripathi M, et al. Endocr Pract 2021;27(1):71-6.

⁸Bashir B, et al. Metabolites. 2023;(5):621.

⁹Davidson M, et al. J Clin Lipidol. 2018;12(4):898-907.e2.

¹⁰Gouni-Berthold I. J Endocr Soc. 2019;4(2):bvz035.

¹¹Paquette M, et al. Atherosclerosis. 2019;283:137-142.

¹²Williams L, et al. J Clin Lipidol. 2018;4:908-919.

 View original content to download multimedia: <https://www.prnewswire.com/news-releases/ionis-presents-positive-results-from-phase-3-balance-study-of-olezarsen-for-familial-chylomicronemia-syndrome-302109871.html>

SOURCE Ionis Pharmaceuticals, Inc.