Positive olezarsen Phase 3 data in familial chylomicronemia syndrome to be presented at 2024 American College of Cardiology (ACC) annual meeting

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– First presentation of pivotal results showing significant reduction in triglycerides and substantial reduction in acute pancreatitis events in patients with rare, life-threatening disease, for which there are no approved treatment options in U.S. –

CARLSBAD, Calif., March 25, 2024 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) announced today that it will present positive Phase 3 Balance results in patients with familial chylomicronemia syndrome (FCS) for the company's lead independent, investigational medicine, olezarsen, at the 2024 American College of Cardiology (ACC) Annual Meeting in Atlanta, Georgia.

The oral presentation will take place on April 7, 2024 at 10:08am ET during the session on Prevention and Health Promotion and the Year in Review. Ionis previously announced positive topline results. As previously shared, monthly dosing of olezarsen 80 mg met the primary endpoint with a statistically significant reduction in triglyceride levels at six months, demonstrated robust reductions in apolipoprotein C-III (apoC-III) and marked reductions in acute pancreatitis (AP) events versus placebo. Olezarsen also demonstrated a favorable safety and tolerability profile.

In addition, 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" will be presented on April 7, 2024 at 8:30am ET during the session on Late-Breaking Clinical Trials II.

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 **LI**gand **C**onjugated **A**ntisense (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.

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.

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Hayley Soffer, 760-603-4679; IR Contact: Wade Walke, 760-603-2331