Ionis initiates pivotal Phase 3 clinical study of olezarsen in patients with severe hypertriglyceridemia

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- More than 3 million people in the US have severe hypertriglyceridemia
- The CORE Phase 3 clinical study further expands Ionis' late-stage pipeline and is the second Phase 3 clinical study in Ionis' broad olezarsen development program
- Olezarsen is one of Ionis' wholly owned medicines the company plans to commercialize

CARLSBAD, Calif., Nov. 2, 2021 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), the leader in RNA-targeted therapies, announced today the initiation of CORE, the second Phase 3 clinical study of olezarsen, formerly known as IONIS-APOCIII-L_{Rx}. The CORE study is evaluating olezarsen in people with severe hypertriglyceridemia (triglyceride levels ≥ 500 mg/dL). Severe hypertriglyceridemia is a life-threatening condition associated with high levels of apoC-III and chylomicronemia, which lead to higher rates of acute pancreatitis, higher risk of cardiovascular disease, and has a high morbidity rate.

"Severe hypertriglyceridemia is a common condition that affects millions of people around the world, including more than 3 million in the US," said Sotirios "Sam" Tsimikas, M.D., senior vice president, clinical development and cardiovascular franchise leader at Ionis. "Initiating the CORE study is a major step in realizing the full potential of olezarsen to treat the range of conditions related to elevated triglycerides associated with high levels of the apoC-III protein."

Olezarsen is an investigational antisense medicine that uses Ionis' **LI**gand-**C**onjugated **A**ntisense, or LICA, technology. It is designed to inhibit the production of apoC-III for patients who are at risk for cardiometabolic disease and acute pancreatitis due to elevated triglyceride levels. ApoC-III is a protein produced in the liver that regulates triglyceride metabolism in the blood.

CORE is a global, double-blind, randomized, placebo-controlled, registrational, Phase 3 study in patients with severe hypertriglyceridemia. It is designed to compare olezarsen to placebo in patients with triglyceride levels equal to or greater than 500 mg/dL who are on the current available standard of care therapies for elevated triglycerides. The primary endpoint of the study is the percent change in fasting triglycerides from baseline at month 6. Secondary endpoints include: percent change from baseline in triglycerides at month 12; proportion of patients who achieve fasting triglycerides less than 500 mg/dL, 880mg/dL and/or 1000 mg/dL and percent change from baseline in other atherogenic lipids at months 6 and 12; and adjudicated acute pancreatitis event rates.

In a Phase 2 clinical study, results showed that olezarsen met its primary and key secondary endpoints with significant reductions in triglyceride and apoC-III levels, and a favorable safety and tolerability profile in the treatment of patients with hypertriglyceridemia (≥200 to ≤500 mg/dL) who have established cardiovascular disease or are at risk for cardiovascular disease. In addition, 91% of subjects achieved a normal triglyceride level of <150 mg/dL.

The broad olezarsen development program aims to enhance the full profile of olezarsen and enroll more than 1500 patients. CORE is one of several clinical studies aimed at evaluating olezarsen's potential to treat diseases caused by high triglycerides. BALANCE, a Phase 3 clinical study evaluating olezarsen in people with familial chylomicronemia syndrome or FCS, is on track for a data readout in 2023.

For more information on the CORE clinical study (NCT05079919) please visit www.clinicaltrials.gov.

About Ionis Pharmaceuticals, Inc.

For more than 30 years, Ionis has been the leader in RNA-targeted therapy, pioneering new markets and changing standards of care with its novel antisense technology. Ionis currently has three marketed medicines and a premier late-stage pipeline highlighted by industry-leading neurological and cardiometabolic franchises. Our scientific innovation began and continues with the knowledge that sick people depend on us, which fuels our vision of becoming one of the most successful biotechnology companies.

To learn more about Ionis, visit www.ionispharma.com and follow us on twitter @ionispharma.

Ionis' Forward-looking Statement

This press release includes forward-looking statements regarding Ionis' business, and the therapeutic and commercial potential of olezarsen and 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 related to the impact COVID-19 could have on our business, and 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. 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, 2020, and the most recent Form 10-Q quarterly filing, which are on file with the SEC. Copies of these and other documents are available from the Company.

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