Ionis announces initiation of the global Phase 3 BALANCE study for AKCEA-APOCIII-LRX in patients with familial chylomicronemia syndrome

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CARLSBAD, Calif., Dec. 1, 2020 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS) today announced the initiation of the Phase 3 BALANCE study for AKCEA-APOCIII-L_{Rx} in adult patients with familial chylomicronemia syndrome (FCS). FCS is a debilitating genetic disease characterized by severely high plasma levels of triglycerides and a risk of unpredictable and potentially fatal acute pancreatitis. In addition to acute pancreatitis, FCS patients are at risk of chronic complications due to permanent organ damage, including chronic pancreatitis and pancreatogenic diabetes. AKCEA-APOCIII-L_{Rx} is designed using Ionis' proprietary **Li**gand **C**onjugated **A**ntisense (LICA) technology platform and is designed to inhibit production of apolipoprotein C-III (apoC-III), a protein produced in the liver that plays a central role in the regulation of serum triglycerides.

"Initiation of the Phase 3 BALANCE study is a significant milestone for the FCS patient community and for our company. This study also reflects our continuing commitment to develop novel treatment options for patients with unmet medical needs such as those living with FCS," said Richard S. Geary, Ph.D., executive vice president of development. "AKCEA-APOCIII-L_{Rx} is the second Ionis antisense medicine that we are developing with FCS patients in mind. We are hopeful about the prospect of bringing forward a new, safe, and effective treatment since these patients have limited available options."

The Phase 3 BALANCE study is a global, multi-center, randomized, double-blind, placebo-controlled study enrolling up to 60 patients (age 18 and over) with FCS. Participants will be randomized in a 2:1 ratio to receive AKCEA-APOCIII-L_{Rx} or placebo via subcutaneous injection once every four weeks for a total 53-week treatment period. The primary endpoint is percent change from baseline in fasting triglyceride levels at six months compared to placebo. Following the treatment period, eligible patients will have the option of enrolling in an open-label extension study. In addition to FCS, Ionis is evaluating additional indications for AKCEA-APOCIII-L_{Rx} development. More information on the BALANCE study is available at www.clinicaltrials.gov/NCT04568434.

AKCEA-APOCIII-L_{Rx} is one of 20 potentially transformative antisense programs in the growing Ionis-owned pipeline that the company is prioritizing and preparing for commercialization. Learn more about some of these programs at Ionis' Virtual Investor Day on Dec. 7, 2020 at 11 a.m. EST.

About FCS
FCS is an ultra-rare disease caused by impaired function of the enzyme lipoprotein lipase (LPL) and characterized by severe hypertriglyceridemia (>880mg/dL or 10mmol/L) and a risk of unpredictable and potentially fatal acute pancreatitis. Because of limited LPL production or function, people with FCS cannot breakdown chylomicrons, lipoprotein particles that are 90 percent triglycerides. In addition to pancreatitis, FCS patients are at risk of chronic complications due to permanent organ damage, including chronic pancreatitis and pancreatogenic (type 3c) diabetes. They can experience daily symptoms including abdominal pain, generalized fatigue and impaired cognition that affect their ability to work. People with FCS also report major emotional and psychosocial effects including anxiety, social withdrawal, depression and brain fog. Additional information on FCS is available at www.fcsfocus.com, through Action FCS at https://www.actionfcs.org/ and through The FCS Foundation at http://www.livingwithfcs.org. For a full list of organizations supporting the FCS community worldwide, please click here.

ABOUT AKCEA-APOCIII-L_{Rx}
AKCEA-APOCIII-L_{Rx} is an investigational antisense medicine designed to reduce the production of apolipoprotein C-III, or apoC-III. ApoC-III is a protein produced in the liver that plays a central role in the regulation of serum triglycerides. Genetically reduced levels of apoC-III are correlated to lower levels of triglycerides and lower risk of cardiovascular disease whereas elevated levels of apoC-III correlate with high triglyceride levels that have been associated with multiple metabolic abnormalities, such as insulin resistance and/or metabolic syndrome as well as elevated cardiovascular event risk. AKCEA-APOCIII-L_{Rx} was developed using Ionis' advanced **LI**gand **C**onjugated **A**ntisense (LICA) technology platform. AKCEA-APOCIII-L_{Rx} is in Phase 3 development for patients with FCS, with plans to evaluate AKCEA-APOCIII-L_{Rx} in patients with other hypertriglyceridemia disorders. AKCEA-APOCIII-L_{Rx} was discovered and developed by Ionis.

ABOUT IONIS PHARMACEUTICALS, INC.
As the leader in RNA-targeted drug discovery and development, Ionis has created an efficient, broadly applicable, drug discovery platform called antisense technology that can treat diseases where no other therapeutic approaches have proven effective. Our drug discovery platform has served as a springboard for actionable promise and realized hope for patients with unmet needs. We created the first and only approved treatment for children and adults with spinal muscular atrophy as well as the world's first RNA-targeted therapeutic approved for the treatment of polyneuropathy in adults with hereditary transthyretin amyloidosis. Our sights are set on all the patients we have yet to reach with a pipeline of more than 40 novel medicines designed to potentially treat a broad range of diseases, including neurological, cardio-renal, metabolic, infectious, and pulmonary diseases. To learn more about Ionis visit www.ionispharma.com and follow us on Twitter @ionispharma.

FORWARD-LOOKING STATEMENT
This press release includes forward-looking statements regarding Ionis' business and the therapeutic and commercial potential of AKCEA-APOCIII-L_{Rx} and Ionis' technologies and products in development, including the business of Akcea Therapeutics, Inc., Ionis' wholly owned subsidiary. 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, 2019, 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.

View original content to download multimedia:http://www.prnewswire.com/news-releases/ionis-announces-initiation-of-the-global-phase-3-balance-study-for-akcea-apociii-lrx-in-patients-with-familial-chylomicronemia-syndrome-301183111.html

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