

Akcea and Ionis report positive topline phase 2 study results of AKCEA-ANGPTL3-LRx

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Favorable safety and tolerability were observed

Primary and multiple secondary endpoints were met with significant reduction in triglyceride levels, additional lipid parameters and ANGPTL3

BOSTON and CARLSBAD, Calif., Jan. 28, 2020 (GLOBE NEWSWIRE) -- Akcea Therapeutics, Inc. (NASDAQ: AKCA), a majority-owned affiliate of Ionis Pharmaceuticals, Inc., and Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), today announced positive topline results from the Phase 2 study of AKCEA-ANGPTL3-LRx in patients with hypertriglyceridemia, type 2 diabetes and non-alcoholic fatty liver disease (NAFLD). The study met the primary endpoint of significant triglyceride lowering and multiple secondary endpoints with a favorable safety and tolerability profile. AKCEA-ANGPTL3-LRx is an investigational antisense oligonucleotide therapy being developed to treat patients with certain cardiovascular and metabolic diseases.

The objective of the dose-ranging Phase 2 study was to evaluate the safety and efficacy of AKCEA-ANGPTL3-LRx. The multicenter, randomized, double-blind, placebo-controlled study included 105 patients with hypertriglyceridemia, type 2 diabetes and NAFLD. Participants were administered AKCEA-ANGPTL3-LRx or placebo via subcutaneous injection for six months. Weekly and monthly dosing was explored in three cohorts with doses ranging from 40 mg to 80 mg of total monthly dose. Observations from the AKCEA-ANGPTL3-LRx study included:

- Statistically significant dose-dependent reductions in fasting triglycerides compared to placebo at all dose levels
- Dose-dependent reductions in ANGPTL3, apoC-III, very low-density lipoprotein (VLDL-C), non-HDL cholesterol and total cholesterol compared to placebo
- No reductions in liver fat or hemoglobin A1C compared to placebo
- AKCEA-ANGPTL3-LRx was generally well-tolerated and demonstrated a favorable safety and tolerability profile. The most common adverse event was injection site reactions, which were mostly mild
- Changes in platelets were similar between placebo and treated groups

Detailed results from this study will be presented at a future medical congress.

"Results from the Phase 2 study showed that antisense-mediated reduction of ANGPTL3 has the potential to address unmet needs in patients with cardiovascular diseases. We are very grateful to the patients, families and physicians who participated in this study and are pleased to share the data with Pfizer, who will determine strategies for potential future development of AKCEA-ANGPTL3-LRx," said Louis O'Dea, chief medical officer at Akcea Therapeutics. "This Phase 2 study further validates the advantages of the LICA technology platform for large indications like cardiovascular disease. We are pleased that we continue to see consistent performance with low volume monthly doses across our LICA programs in terms of efficacy, safety and patient tolerability."

ABOUT AKCEA-ANGPTL3-LRx

AKCEA-ANGPTL3-LRx is an investigational antisense therapy being developed to treat patients with certain cardiovascular and metabolic diseases. This antisense medicine is designed to reduce the production of angiopoietin-like 3 (ANGPTL3) protein in the liver, a key regulator of triglycerides, cholesterol, glucose and energy metabolism. AKCEA-ANGPTL3-LRx was developed using Ionis' advanced **L**igand **C**onjugated **A**ntisense (LICA) technology platform. The potential therapeutic benefits of ANGPTL3 reduction are supported by the discovery that people with a genetic deficiency in ANGPTL3 have reduced levels of low-density lipoprotein cholesterol (LDL-C) and triglycerides, and a decreased risk of diabetes and cardiovascular disease.¹ In a Phase 1/2 study, patients treated with AKCEA-ANGPTL3-LRx achieved robust, dose-dependent reductions of ANGPTL3, triglycerides, LDL-cholesterol and total cholesterol with a positive safety and tolerability profile.² AKCEA-ANGPTL3-LRx was discovered by Ionis and has been co-developed by Akcea and Ionis.

In November 2019, Akcea announced the closing of the worldwide exclusive licensing agreement with Pfizer Inc. for AKCEA-ANGPTL3-LRx. Under terms of the agreement Akcea and Ionis received a \$250 million upfront license fee, which was split equally between the two companies. Pfizer is responsible for all development and regulatory activities and costs beyond those associated with this Phase 2 study. Akcea and Ionis are also eligible to receive development, regulatory and sales milestone payments of up to \$1.3 billion and tiered, double-digit royalties on annual worldwide net sales.

ABOUT AKCEA THERAPEUTICS

Akcea Therapeutics, Inc., a majority-owned affiliate of Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), is a biopharmaceutical company focused on developing and commercializing drugs to treat patients with serious and rare diseases. Akcea is commercializing TEGSEDI[®] (inotersen) and WAYLIVRA[®] (volanesorsen), as well as advancing a mature pipeline of novel drugs, including AKCEA-APO(a)-LRx, AKCEA-ANGPTL3-LRx, AKCEA-APOCIII-LRx, and AKCEA-TTR-LRx, with the potential to treat multiple diseases. All six drugs were discovered by Ionis, a leader in antisense therapeutics, and are based on Ionis' proprietary antisense technology. TEGSEDI is approved in the U.S., E.U., Canada and Brazil. WAYLIVRA is approved in the E.U. and is currently in Phase 3 clinical development for the treatment of people with familial partial lipodystrophy, or FPL. Akcea is building the infrastructure to commercialize its drugs globally. Akcea is a global company headquartered in Boston, Massachusetts. Additional information about Akcea is available at www.akceatx.com and you can follow us on Twitter at @akceatx.

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 disease, including neurological, cardiovascular, infectious, and pulmonary diseases. To learn more about Ionis visit www.ionispharma.com and follow us on Twitter @ionispharma.

AKCEA AND IONIS FORWARD-LOOKING STATEMENT

This press release includes forward-looking statements regarding the business of Akcea Therapeutics, Inc. and Ionis Pharmaceuticals, Inc. and the therapeutic and commercial potential of AKCEA-ANGPTL3-L_{RX}. Any statement describing Akcea's or Ionis' goals, expectations, financial or other projections, intentions or beliefs, including the commercial potential of AKCEA-ANGPTL3-L_{RX} or other of Akcea's or Ionis' drugs in development is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such drugs. Akcea's and 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 Akcea's and Ionis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Akcea and Ionis. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Akcea's and Ionis' programs are described in additional detail in Akcea's and Ionis' quarterly reports on Form 10-Q and annual reports on Form 10-K, which are on file with the SEC. Copies of these and other documents are available from each company.

In this press release, unless the context requires otherwise, "Ionis," "Akcea," "Company," "Companies," "we," "our," and "us" refers to Ionis Pharmaceuticals and/or Akcea Therapeutics.

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