Akcea and Ionis Report Positive Phase 1/2a Data with AKCEA-APOCIII-LRx

October 31, 2017

Akcea expects to initiate Phase 2b in patients with hypertriglyceridemia with established cardiovascular disease by the end of this year

CAMBRIDGE, Mass., Oct. 31, 2017 (GLOBE NEWSWIRE) -- Akcea Therapeutics, Inc. (NASDAQ:AKCA), an affiliate of Ionis Pharmaceuticals, Inc. (NASDAQ:IONS), today announced positive results of a Phase 1/2a clinical study with AKCEA-APOCIII-L_{Rx}. Akcea is focused on developing and commercializing drugs to treat patients with serious cardiometabolic diseases caused by lipid disorders.

"In this first-in-human study, AKCEA-APOCIII-L_{Rx} achieved substantial sustained reductions of apoC-III and triglyceride levels. These data reinforce the consistency and predictability of target reduction with significantly lower doses using Ionis' LICA technology, very similar to recently reported results from AKCEA-APO(a)-L_{Rx} and AKCEA-ANGPTL3-L_{Rx}," said Dr. Louis O'Dea, chief medical officer at Akcea Therapeutics. "Based on the positive results from this study, we plan to initiate a Phase 2b dose-ranging study by the end of this year to choose the optimal dose and dose schedule for a Phase 3 cardiovascular outcome study."

AKCEA-APOCIII-L_{Rx} is part of a strategic collaboration with Novartis to develop and co-commercialize AKCEA-APO(a)-L_{Rx} and AKCEA-APOCIII-L_{Rx}. Under the terms of the collaboration, if Novartis exercises its option after successful completion of the Phase 2, they will be responsible for a global Phase 3 cardiovascular outcome study in a high-risk population as well as worldwide development and, if approved, co-commercialization activities.

In a Phase 1/2a clinical study in healthy volunteers and patients with elevated triglyceride levels, treatment with multiple doses of AKCEA-APOCIII-L_{Rx} resulted in dose-dependent reductions in apoC-III protein of up to 84% after six weeks of treatment. Treatment with AKCEA-APOCIII-L_{Rx} also resulted in dose-dependent reductions in triglycerides of up to 71%. Significant dose-dependent reductions of up to 30% in apolipoprotein B (apoB) and increases of up to 100% in high-density lipoprotein cholesterol (HDL-C), were also observed. Both decreased levels of apoB and increased levels of HDL-C are associated with decreased cardiovascular risk. AKCEA-APOCIII-L_{Rx} was well tolerated in the study. No serious adverse events, including no significant changes in platelet count, and no adverse events leading to treatment discontinuation were observed. The safety and tolerability profile of AKCEA-APOCIII-L_{Rx} in this study supports continued development.

AKCEA-APOCIII-L_{Rx} inhibits the production of apolipoprotein C-III (ApoC-III) for the broad population of patients who have cardiometabolic disease due to their elevated triglyceride levels and ApoC-III. Ionis' **LI**gand **C**onjugated **A**ntisense, or LICA, conjugates specific chemical structures or molecules to antisense drugs to increase the efficiency of drug uptake in a particular tissue. The enhancements from the LICA technology have the potential to allow for less frequent administration and significantly lower doses providing greater patient convenience.

ABOUT THE AKCEA AND NOVARTIS COLLABORATION

In January 2017, Akcea and Ionis entered into an exclusive, worldwide option and collaboration agreement with Novartis to develop and commercialize AKCEA-APOCIII-L_{Rx} and AKCEA-APO(a)-L_{Rx}. Akcea plans to complete the ongoing Phase 2 dose-ranging study for AKCEA-APO(a)-L_{Rx} in patients with high lipoprotein(a), or Lp(a), with established cardiovascular disease and to initiate a Phase 2 dose-ranging study for AKCEA-APOCIII-L_{Rx} in patients with hypertriglyceridemia and established cardiovascular disease. Both studies are being conducted to choose the optimal dose and evaluate alternative dose schedules, such as monthly dosing, for Phase 3 cardiovascular outcomes studies. Following the successful completion of each Phase 2 dose-ranging study, and prior to initiation of the Phase 3 study, Novartis has the option to license and commercialize each drug. For each drug, upon option exercise, Novartis will pay Akcea a $150 million license fee of which 50% will be paid to Ionis. Upon licensing, Novartis plans to conduct a global Phase 3 cardiovascular outcome study in high-risk patients. Novartis will be responsible for worldwide development and, if approved, co-commercialization activities. Akcea retains the right to co-commercialize any successful drug through its specialty sales force focused on lipid specialists on terms and conditions to be agreed with Novartis.

ABOUT APOC-III AND TRIGLYCERIDES

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. Elevated levels of apoC-III correlate with high triglycerides associated with multiple metabolic abnormalities, such as insulin resistance and/or metabolic syndrome.

ABOUT AKCEA THERAPEUTICS

Akcea Therapeutics, an affiliate of Ionis Pharmaceuticals, Inc., is a biopharmaceutical company focused on developing and commercializing drugs to treat patients with serious cardiometabolic diseases caused by lipid disorders. Akcea is advancing a mature pipeline of four novel drugs, including volanesorsen, AKCEA-APO(a)-L_{Rx}, AKCEA-ANGPTL3-L_{Rx} and AKCEA-APOCIII-L_{Rx}, all with the potential to treat multiple diseases. All four drugs were discovered by and are being co-developed with Ionis, a leader in antisense therapeutics, and are based on Ionis' proprietary antisense technology. The most advanced drug in its pipeline, volanesorsen, is under regulatory review in the U.S., EU and Canada for the treatment of familial chylomicronemia syndrome, or FCS, and is currently in Phase 3 clinical development for the treatment of familial partial lipodystrophy, or FPL. Akcea is building the infrastructure to commercialize its drugs globally with a focus on lipid specialists as the primary call point. Akcea is located in Cambridge, Massachusetts. Additional information about Akcea is available at www.akceatx.com.

FORWARD-LOOKING STATEMENT

This press release includes forward-looking statements regarding the business of Akcea Therapeutics, Inc. and the therapeutic and commercial potential of volanesorsen and other products in development. Any statement describing Akcea's 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, 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 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 forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Akcea. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Akcea's programs are described in additional detail in its final prospectus for its initial public offering and its most recent quarterly report on Form 10-Q, which is on file with the SEC.

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.

Media and Investor Contact:
Kathleen Gallagher
Executive Director, Corporate Communications and Investor Relations
617-207-8509
kgallagher@akceatx.com

Source: Akcea Therapeutics, Inc.