

Akcea Completes Enrollment in Phase 2b Study of AKCEA-APO(a)-LRx

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CAMBRIDGE, Mass., Feb. 07, 2018 (GLOBE NEWSWIRE) -- Akcea Therapeutics, Inc. (NASDAQ:AKCA), today announced it had completed enrollment of a Phase 2b clinical study of investigational drug AKCEA-APO(a)-LRx. Akcea is conducting the study in patients with high Lp(a) and established cardiovascular disease (CVD) to determine the dose level and frequency of administration for a future planned Phase 3 cardiovascular outcome study and to determine the safety and tolerability profile of AKCEA-APO(a)-LRx. Akcea plans to report top-line data from the Phase 2b study in the second half of 2018. Akcea is an affiliate of Ionis Pharmaceuticals Inc. focused on developing and commercializing drugs to treat patients with serious cardiometabolic diseases caused by lipid disorders.

AKCEA-APO(a)-LRx is part of a strategic collaboration with Novartis. If Novartis exercises its option to license AKCEA-APO(a)-LRx after successful completion of the Phase 2b study, it will be responsible for all future development activities for AKCEA-APO(a)-LRx including a global Phase 3 cardiovascular outcome study and, if approved, global commercialization activities. As part of the agreement, Akcea retains the right to co-commercialize globally.

"Elevated Lp(a) is a genetic trait that is present in approximately 20-30% of the population and is recognized as a risk factor for cardiovascular disease. There are currently no treatment options available that specifically target Lp(a). AKCEA-APO(a)-LRx is the only program in clinical development for this indication that has been shown to substantially lower Lp(a)," said Mustafa Noor, MD, chief development officer of Akcea Therapeutics. "We now look forward to completing the study and beginning analysis of the study data. The results of this study will help us better understand the efficacy and safety profile of AKCEA-APO(a)-LRx, so that this program can advance into a pivotal cardiovascular outcome study to determine the potential benefit of lowering Lp(a)."

AKCEA-APO(a)-LRx is an antisense drug that uses Ionis' advanced **L**igand **C**onjugated **A**ntisense, or LICA technology. AKCEA-APO(a)-LRx inhibits the production of apolipoprotein(a), or Apo(a), protein, thereby reducing lipoprotein(a), or Lp(a). Lp(a) is made up of apo(a) protein bound to LDL cholesterol resulting in an atherogenic and thrombogenic lipoprotein that has been genetically validated as an independent risk factor for coronary artery disease, heart attack, stroke, calcific aortic valve disease and peripheral arterial disease. Phase 1 studies of all three of Akcea's LICA drugs have shown that doses up to 30-fold lower than non-LICA drugs result in consistent target reductions and a favorable safety and tolerability profile.

The randomized, double-blind, placebo-controlled, dose-ranging Phase 2b study is evaluating the safety and efficacy of different doses of AKCEA-APO(a)-LRx. The study enrolled over 270 patients with high Lp(a) and established cardiovascular disease. For further study information, please visit www.clinicaltrials.gov and search for AKCEA-APO(a)-LRx.

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-LRx and AKCEA-APO(a)-LRx. Akcea is conducting a Phase 2 dose-ranging study for AKCEA-APO(a)-LRx in patients with high lipoprotein(a), or Lp(a), with established cardiovascular disease with data planned in 2018 and a Phase 2b dose-ranging study for AKCEA-APOCIII-LRx in patients with hypertriglyceridemia and established cardiovascular disease with data planned in 2019. The goal of both studies is to choose the optimal dose and evaluate alternative dose schedules, such as monthly dosing, for Phase 3 cardiovascular outcomes studies. Novartis has the option to license each drug after successful completion of the Phase 2 dose-ranging study and end-of-Phase 2 meeting with FDA. Upon option exercise for each drug, Novartis will pay Akcea a \$150 million license fee of which 50% will be paid to Ionis. If licensed, 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 Lp(a)

Elevated Lp(a) is recognized as an independent, genetic cause of cardiovascular disease. Lp(a) levels are determined at birth and, therefore, lifestyle modification, including diet and exercise, do not impact Lp(a) levels. Currently, there is no effective drug therapy to target and reduce elevated levels of Lp(a). Additional information is available from the Lipoprotein(a) Foundation at <http://www.lipoproteinafoundation.org/>.

In a Phase 1/2 study with AKCEA-APO(a)-LRx in patients with elevated levels of Lp(a), significant and sustained reductions in Lp(a) of up to 97% were observed, with a mean reduction of 79% after only a single, small volume dose of AKCEA-APO(a)-LRx. With multiple doses of AKCEA-APO(a)-LRx, even greater reductions of Lp(a) of up to 99% were observed, with a mean reduction of 92%. AKCEA-APO(a)-LRx was generally safe and well tolerated in the study, which supported continued development. Out of 165 injections, there were no injection site reactions or flu-like symptoms reported. To review the full study results published in *The Lancet*, [click here](#).

ABOUT AKCEA THERAPEUTICS

Akcea Therapeutics, an affiliate of Ionis Pharmaceuticals, Inc. (NASDAQ:IONS), 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)-LRx, AKCEA-ANGPTL3-LRx and AKCEA-APOCIII-LRx, 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 AKCEA-APO(a)-LRx 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.

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