Akcea Initiates Phase 2 Study of AKCEA-APO(a)-L Rx in Patients with High Lp(a) and Cardiovascular Disease

CAMBRIDGE, Mass., March 30, 2017 /PRNewswire/ -- Akcea Therapeutics, a subsidiary of Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), today announced the initiation of a Phase 2b dose-ranging study of AKCEA-APO(a)-LRx in patients with hyperlipoproteinemia(a) and established cardiovascular disease. The goal of the study is to determine the dose level and frequency for use of AKCEA-APO(a)-LRx in a planned Phase 3 cardiovascular outcome study.

AKCEA-APO(a)-LRx is part of Akcea's strategic collaboration with Novartis to develop and commercialize drugs to treat patients who are at high cardiovascular risk due to inadequately treated lipid disorders. AKCEA-APO(a)-LRx inhibits the production of apolipoprotein(a), or Apo(a) protein, thereby reducing lipoprotein(a), or Lp(a). Apo(a) is a very atherogenic and thrombogenic form of low-density lipoprotein (LDL). Elevated Lp(a) is recognized as an independent, genetic cause of coronary artery disease, heart attack, stroke and peripheral arterial disease. AKCEA-APO(a)-LRx is an antisense drug that uses Ionis' advanced LIgand Conjugated Antisense, or LICA technology. The enhancements offered by Ionis' LICA technology can potentially provide greater patient convenience by allowing for significantly lower doses and less frequent administration as compared to non-LICA drugs.

"There is currently no effective drug therapy to specifically and robustly lower elevated levels of Lp(a), which is recognized as an independent, genetic cause of cardiovascular disease. We believe addressing elevated Lp(a) is the next important horizon in lipid-focused therapy and, through our collaboration and option agreement with Novartis, we plan to develop AKCEA-APO(a)-LRx to treat patients with established cardiovascular disease in whom elevated Lp(a) plays a causal role in their disease," said Paula Soteropoulos, chief executive officer at Akcea Therapeutics. "Following the achievement of specified development milestones and prior to the initiation of a Phase 3 study, Novartis will be able to exercise its option to license the drug. Upon licensing, Novartis will be responsible for worldwide development and commercialization of AKCEA-APO(a)-LRx."

The randomized, double-blind, placebo-controlled, dose-ranging Phase 2b study will evaluate the safety and efficacy of different doses of AKCEA-APO(a)-LRx in approximately 270 patients with hyperlipoproteinemia(a) and established cardiovascular disease. Akcea plans to report top-line data from this study in the middle of 2018. For further study information, please visit www.clinicaltrials.gov and search for AKCEA-APO(a)-LRx.

In January 2017, Ionis and Akcea initiated a strategic collaboration and option agreement with Novartis to develop and commercialize AKCEA-APO(a)-LRx and AKCEA-APOCIII-LRx. This collaboration can accelerate Akcea's ability to deliver these potential therapies to the large populations of patients who have high cardiovascular risk due to inadequately treated lipid disorders. Ionis and Akcea have received a $75 million upfront option payment and a $100 million equity investment in Ionis. Novartis has also agreed to purchase an additional $50 million in Akcea equity. For each drug, upon option exercise, Novartis will pay Ionis and Akcea a $150 million license fee, will initiate a global Phase 3 cardiovascular outcome study in high-risk patients and will be responsible for worldwide development and commercialization activities, if approved. Akcea plans to co-commercialize any licensed drug commercialized by Novartis 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 specifically and robustly lower elevated levels of Lp(a). Additional information is available from Lipoprotein(a) Foundation at 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.

ABOUT AKCEA THERAPEUTICS
Akcea Therapeutics is a late-stage pharmaceutical 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 with the potential to treat multiple diseases, including volanesorsen, AKCEA-APO(a)-LRx, AKCEA-ANGPTL3-LRx and AKCEA-APOCIII-LRx, which are all based on antisense technology developed by Ionis Pharmaceuticals, Inc. The most advanced drug in its pipeline, volanesorsen, has completed a Phase 3 clinical program 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 assembling the infrastructure to commercialize its drugs globally with a focus on lipid specialists as the primary call point. Akcea is a subsidiary of Ionis Pharmaceuticals, Inc. and 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., a subsidiary of Ionis Pharmaceuticals, 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 Ionis Pharmaceuticals, Inc.'s annual report on Form 10-K for the year ended December 31, 2016, 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.

To view the original version on PR Newswire, visit: http://www.prnewswire.com/news-releases/akcea-initiates-phase-2-study-of-akcea-apoa-l-rx-in-patients-with-high-lpa-and-cardiovascular-disease-300431582.html

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