Akcea and Ionis Announce Late-Breaking Presentation of Data From AKCEA-APO(a)-LRx at the American Heart Association Scientific Sessions

November 8, 2018

Results to be presented show a significant reduction of Lp(a) levels, favorable safety and tolerability profile

BOSTON and CARLSBAD, Calif., Nov. 08, 2018 (GLOBE NEWSWIRE) -- Akcea Therapeutics, Inc. (NASDAQ: AKCA), an affiliate of Ionis Pharmaceuticals, Inc., and Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), today announced that clinical data on AKCEA-APO(a)-L_{Rx} in patients with established cardiovascular disease (CVD) and elevated levels of lipoprotein(a), or Lp(a), will be presented at the American Heart Association Scientific Sessions in Chicago November 10-12, 2018. AKCEA-APO(a)-L_{Rx} is an antisense drug developed using Ionis' proprietary **LI**gand **C**onjugated **A**ntisense, or LICA technology platform.

AKCEA-APO(a)-L_{Rx} is designed to inhibit production of apolipoprotein(a), or Apo(a) protein, thereby reducing systemic levels of lipoprotein(a), or Lp(a). Elevated Lp(a) is an independent, hereditary risk factor for CVD that cannot be well controlled with lifestyle modifications, such as diet or exercise, or with treatment using existing cholesterol-lowering therapies. It is estimated that there are 8 to 10 million treatable patients living with cardiovascular disease and elevated levels of Lp(a).

Following is information about the late-breaking presentation of AKCEA-APO(a)-L_{Rx}:

Saturday, November 10, 2018 from 4:15-4:25 pm CDT

- Safety and Efficacy of AKCEA-APO(a)-L_{Rx} to Lower Lipoprotein(a) Levels in Patients With Established Cardiovascular Disease: A Phase 2 Dose-Ranging Trial will be presented by Sotirios Tsimikas, M.D., FACC, FAHA, FSCAI, Univ California San Diego, and vice president of global cardiovascular development at Ionis Pharmaceuticals, La Jolla, CA (Session LBS.02 – Late Breaking Clinical Trial: Novel Approaches to CV Prevention; Main Event 1)

Akcea will have an on-site presence at the meeting at booth 826 in the Science & Technology Hall where attendees can learn more about TEGSEDI™ (inotersen).

ABOUT AKCEA-APO(a)-L_{Rx} AND THE PHASE 2 STUDY

Akcea and Ionis announced positive topline results in September 2018 from the Phase 2 study demonstrating a significant reduction in Lp (a) and a favorable safety and tolerability profile. Results from the study showed most patients in the active group achieved Lp(a) reductions below the established threshold of risk for cardiovascular disease events. The Phase 2 randomized, double-blind, placebo-controlled, dose-ranging study evaluated the safety and efficacy of different doses of AKCEA-APO(a)-L_{Rx} in 286 patients with elevated levels of Lp(a) and established cardiovascular disease. The study had a five to one randomization testing different doses and dose frequencies of AKCEA-APO(a)-L_{Rx}. Weekly, every other week and monthly doses were tested ranging from 20mg to 60mg. Patients were dosed for at least six months with some patients dosed up to one year. The primary efficacy endpoint was the percent change in Lp(a) from baseline at the primary analysis time point (6 months) compared to placebo.

AKCEA-APO(a)-L_{Rx} is an antisense drug that uses Ionis' advanced **LI**gand **C**onjugated **A**ntisense, or LICA technology. AKCEA-APO(a)-L_{Rx} inhibits the production of apolipoprotein(a), or Apo(a), protein, thereby reducing Lp(a).

ABOUTLp(a)
Lipoprotein(a), or Lp(a) is made up of apo(a) protein bound to LDL cholesterol and contains oxidized phospholipids, resulting in an atherogenic, pro-inflammatory and thrombogenic lipoprotein. Elevated Lp(a) is recognized as an independent, genetic cause of cardiovascular disease present in approximately 20-30% of the population. Lp(a) levels are determined at birth and, therefore, cannot be well controlled with lifestyle modifications, including diet and exercise.

For additional information about Lp(a), please see the Lipoprotein(a) Foundation at http://www.lipoproteinafoundation.org/.

ABOUTTHEAKCEAANDNOVARTISCOLLABORATION
In January 2017, Akcea 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}. Along with the Phase 2 study of AKCEA-APO(a)-L_{Rx} reported here, Akcea is also conducting a Phase 2b dose-ranging study for AKCEA-APOCIII-L_{Rx} 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 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. As part of the collaboration, Akcea has the rights to co-commercialize Akcea-APO(a)-L_{Rx} in selected markets, on mutually agreed terms and conditions.

About AkceaTherapeutics, Inc.
Akcea Therapeutics, Inc., an affiliate of Ionis Pharmaceuticals, Inc., is a biopharmaceutical company focused on developing and commercializing drugs to treat patients with serious and rare diseases. Akcea is advancing a mature pipeline of six novel drugs, including TEGSEDI™ (inotersen), WAYLIVRA™ (volanesorsen), AKCEA-APO(a)-L_{Rx}, AKCEA-ANGPTL3-L_{Rx}, AKCEA-APOCIII-L_{Rx}, and AKCEA-TTR-L_{Rx}, all with the potential to treat multiple diseases. All six drugs were discovered by and are being co-developed with Ionis, a leader in antisense therapeutics, and are based on Ionis' proprietary antisense technology. TEGSEDI is approved in the U.S., E.U. and Canada. WAYLIVRA is under regulatory review for the treatment of familial chylomicronemia syndrome, or FCS, 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.

About Ionis Pharmaceuticals
As the leader in RNA-targeted drug discovery and development, Ionis has created an efficient, broadly applicable, proprietary antisense technology platform with the potential to 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 – such as children and adults with spinal muscular atrophy (SMA). We created SPINRAZA® (nusinersen)* and are proud to have brought new hope to the SMA community by developing the first and only approved treatment for this disease.

Our sights are set on all the patients we have yet to reach with a pipeline of more than 40 drugs with the potential to treat patients with cardiovascular disease, rare diseases, neurological diseases, infectious diseases and cancer. We created TEGSEDI™ (inotersen) the world's first RNA-targeted therapeutic approved for the treatment of polyneuropathy in adult patients with hereditary transthyretin (TTR) amyloidosis (ATTR) that our affiliate, Akcea Therapeutics, is commercializing. Together with Akcea, we are also bringing new medicines to patients with cardiometabolic lipid disorders.

To learn more about Ionis follow us on twitter @ionispharma or visit http://ir.ionispharma.com/.

*Spinraza is marketed by Biogen.

AKCEA AND IONIS FORWARD-LOOKINGSTATEMENT
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-APO(a)-L_{Rx}. Any statement describing Akcea's or Ionis' goals, expectations, financial or other projections, intentions or beliefs, including the commercial potential of AKCEA-APO(a)-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 Ionis' and Akcea's programs are described in additional detail in Ionis' and Akcea's 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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Source: Akcea Therapeutics, Inc.