

## Akcea Initiates Phase 2 Study of AKCEA-ANGPTL3-LRx in Patients with Hypertriglyceridemia, Type 2 Diabetes Mellitus and Nonalcoholic Fatty Liver Disease (NAFLD)

December 14, 2017

CAMBRIDGE, Mass., Dec. 14, 2017 (GLOBE NEWSWIRE) -- Akcea Therapeutics, Inc. (NASDAQ:AKCA), an affiliate of Ionis Pharmaceuticals, Inc., focused on developing and commercializing drugs to treat patients with serious cardiometabolic diseases caused by lipid disorders, today announced the initiation of a Phase 2 program of AKCEA-ANGPTL3-LRx in patients with hypertriglyceridemia, type 2 diabetes mellitus and nonalcoholic fatty liver disease (NAFLD). The primary goal of the study is to determine the dose level and frequency for use of AKCEA-ANGPTL3-LRx in future registration studies.

AKCEA-ANGPTL3-LRx is designed to target and reduce the production of angiopoietin-like 3, or ANGPTL3, a protein produced and secreted by the liver. The congenital absence of ANGPTL3 is associated with lower lipid levels and reduced risk of insulin resistance, diabetes mellitus and cardiovascular disease relative to individuals with normal production of ANGPTL3 protein.

"To date, we have seen that ANGPTL3 modulates multiple lipid parameters that are implicated in a variety of significant metabolic disorders like NAFLD and diabetes, where currently physicians are only able to manage symptoms, placing a major burden on individuals and the healthcare system," said Louis O'Dea, chief medical officer at Akcea Therapeutics. "By conducting Phase 2 studies in patients with these multifactorial diseases with AKCEA-ANGPTL3-LRx we hope to gain critical insights into the role of ANGPTL3 in these diseases."

The multicenter, randomized, double-blind, placebo-controlled, dose-ranging Phase 2b study will evaluate the safety and efficacy of AKCEA-ANGPTL3-LRx administered at different doses and dosing intervals to approximately 144 patients with hypertriglyceridemia, type 2 diabetes mellitus and NAFLD. Akcea plans to report top-line data from this study in 2019. For further study information, please visit [www.clinicaltrials.gov](http://www.clinicaltrials.gov) and search for AKCEA-ANGPTL3-LRx.

### ABOUT AKCEA-ANGPTL3-LRx

AKCEA-ANGPTL3-LRx is a ligand conjugated antisense (LICA) drug designed to reduce angiopoietin-like 3 protein, or ANGPTL3. People with congenital absence of ANGPTL3 have lower LDL-C and triglyceride levels and lower risk of cardiovascular disease. Akcea and Ionis are developing AKCEA-ANGPTL3-LRx to treat patients with multiple lipid disorders, including rare hyperlipidemias and NAFLD with metabolic complications.

In a Phase 1/2 clinical study in volunteers with elevated triglycerides, published in *The New England Journal of Medicine*, treatment with multiple doses of AKCEA-ANGPTL3-LRx resulted in dose-dependent reductions in ANGPTL3 protein greater than 85% after six weeks of treatment. Treatment with AKCEA-ANGPTL3-LRx also resulted in substantial and dose-dependent reductions in triglycerides, LDL cholesterol, VLDL cholesterol, non-HDL cholesterol, apolipoprotein B and apolipoprotein C-III protein. AKCEA-ANGPTL3-LRx was well tolerated in the study. No serious adverse events, no platelet count reductions and no injection site reactions were reported. Further, there were no discontinuations during the treatment period. LICA technology can provide greater patient convenience by allowing for significantly lower doses and less frequent administration, compared to non-LICA drugs. 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.

### 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](http://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, AKCEA-ANGPTL3-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.

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