Akcea Initiates AKCEA-ANGPTL3-LRx Phase 2 Program in Patients with Rare Hyperlipidemias

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CAMBRIDGE, Mass., Nov. 13, 2017 (GLOBE NEWSWIRE) -- Akcea Therapeutics, Inc. (NASDAQ:AKCA), an affiliate of Ionis Pharmaceuticals, Inc. (NASDAQ:IONS), focused on developing and commercializing drugs to treat patients with serious cardiometabolic diseases caused by lipid disorders, today announced the initiation of an exploratory Phase 2 program of AKCEA-ANGPTL3-L_{Rx} in patients with rare hyperlipidemias.

AKCEA-ANGPTL3-L_{Rx} is designed to reduce the production of angiopoietin-like 3, or ANGPTL3. The absence of ANGPTL3 has been shown to be cardioprotective and associated with reduced risk of insulin resistance and diabetes mellitus.

The AKCEA-ANGPTL3-L_{Rx} Phase 2 program is designed to include three clinical studies in patients with one of three rare hyperlipidemias, including familial chylomicronemia syndrome (FCS), familial partial lipodystrophy (FPL), and homozygous familial hypercholesterolemia (HoFH). The objectives of these studies are to determine the pharmacodynamics, pharmacokinetics, safety and tolerability of AKCEA-ANGPTL3-L_{Rx}, and to further characterize the drug's potential in these patient populations.

"ANGPTL3 is a key regulator of a number of lipid and metabolic pathways and as such is an important target for the therapeutic management of rare hyperlipidemias, such as FCS, FPL and HoFH. In FCS, severe elevation of triglycerides results in a high risk of acute and chronic pancreatitis and other metabolic complications. Patients with HoFH are subject to early cardiovascular disease and premature death due to high LDL cholesterol levels. Patients with FPL often have both high triglycerides and high LDL cholesterol levels as well as other complications related to insulin resistance and fatty liver, which can lead to accelerated atherogenesis and liver failure," said Louis O'Dea, chief medical officer at Akcea Therapeutics. "We are committed to developing additional therapeutic options for these patient populations whose significant medical needs are currently greatly underserved."

Consistent with Akcea's commitment to the FCS community, the first study is designed to evaluate the pharmacodynamics, pharmacokinetics, safety and tolerability of AKCEA-ANGPTL3-L_{Rx} in patients with FCS. Study participants will receive AKCEA-ANGPTL3-L_{Rx} by subcutaneous injection once weekly for 13 weeks. Akcea plans to report top-line data from this study in 2018. Akcea plans to initiate similar pilot studies shortly in patients with FPL and patients with HoFH. For further study information, please visit www.clinicaltrials.gov and search for AKCEA-ANGPTL3-L_{Rx}.

ABOUT AKCEA-ANGPTL3-L_{Rx}

AKCEA-ANGPTL3-L_{Rx} is a ligand conjugated antisense (LICA) drug designed to reduce angiopoietin-like 3 protein, or ANGPTL3. ANGPTL3 is a key regulator of triglycerides, cholesterol, glucose and energy metabolism. People with lower levels of ANGPTL3 have lower LDL-C and triglyceride levels and lower risk of heart attacks. Ionis and Akcea are developing AKCEA-ANGPTL3-L_{Rx} to treat 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-L_{Rx} resulted in dose-dependent reductions in ANGPTL3 protein of up to 85% after six weeks of treatment. Treatment with AKCEA-ANGPTL3-L_{Rx} 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-L_{Rx} was well tolerated in the study. No serious adverse events, including platelet count reductions and injection site reactions, were reported. Further, there were no discontinuations during the treatment period. 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., 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.

ABOUT IONIS PHARMACEUTICALS, INC.

Ionis is the leading company in RNA-targeted drug discovery and development focused on developing drugs for patients who have the highest unmet medical needs, such as those patients with severe and rare diseases. Using its proprietary antisense technology, Ionis has created a large pipeline of first-in-class or best-in-class drugs, with over three dozen drugs in development. SPINRAZA® (nusinersen) has been approved in global markets for the treatment of spinal muscular atrophy (SMA). Biogen is responsible for commercializing SPINRAZA. Drugs that have successfully completed Phase 3 studies include inotersen, an antisense drug Ionis is developing to treat patients with hereditary TTR amyloidosis (hATTR), and volanesorsen, an antisense drug discovered by Ionis and co-developed by Ionis and Akcea Therapeutics to treat patients with either familial chylomicronemia syndrome or familial partial lipodystrophy. Akcea, an affiliate of Ionis, is a biopharmaceutical company focused on developing and commercializing drugs to treat patients with serious cardiometabolic diseases caused by lipid disorders. If approved, volanesorsen will be commercialized through Ionis' affiliate, Akcea. Inotersen filings for marketing approval have been submitted in the U.S. and EU. Volanesorsen filings for marketing approval have been submitted in the U.S., EU, and Canada. Ionis' patents provide strong and extensive protection for its drugs and technology. Additional information about Ionis is available at www.ionispharma.com.

AKCEA 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-L_{Rx} 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.

IONIS 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-ANGPTL3-L_{Rx} and other products in development. Any statement describing Ionis' 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. 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 Ionis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Ionis. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Ionis' programs are described in additional detail in Ionis' annual report on Form 10-K for the year ended December 31, 2016, and its most recent quarterly report on Form 10-Q, which are on file with the SEC. Copies of these and other documents are available from the 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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