Akcea and Ionis Announce Initiation of CARDIO-TTRansform Phase 3 Clinical Trial for AKCEA-TTR-LRx in Patients with TTR-mediated Amyloid Cardiomyopathy

January 10, 2020

BOSTON and CARLSBAD, Calif., Jan. 10, 2020 (GLOBE NEWSWIRE) -- Akcea Therapeutics, Inc. (NASDAQ: AKCA), a majority-owned affiliate of Ionis Pharmaceuticals, Inc., and Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), announced today the initiation of the CARDIO-TTRansform Phase 3 cardiovascular outcomes study for AKCEA-TTR-L_{Rx} in patients with transthyretin-mediated amyloid cardiomyopathy (ATTR cardiomyopathy).

"The initiation of our CARDIO-TTRansform Phase 3 trial represents another important milestone further demonstrating Akcea and Ionis' commitment to bring new treatment options to patients around the world living with TTR amyloidosis. Both the wild type and hereditary forms of ATTR cardiomyopathy are underdiagnosed and potentially fatal with limited treatment options available," said Damien McDevitt, Ph.D., interim chief executive officer at Akcea. "We remain very encouraged by the progress of our clinical studies with AKCEA-TTR-L_{Rx} thus far and look forward to working with our team of outstanding global investigators to continue to advance this clinical program in the months ahead."

AKCEA-TTR-L_{Rx} is an antisense drug developed using Ionis' proprietary **LI**gand **C**onjugated **A**ntisense (LICA) technology platform and is designed to inhibit production of TTR. It was discovered by Ionis and is being co-developed by Ionis and Akcea. In a Phase 1 clinical trial, patients treated with AKCEA-TTR-L_{Rx} experienced reductions in TTR of up to 94 percent at the highest dose.

"TTR amyloidosis is an under-recognized cause of heart failure in many adults. While there have been some advances in standard of care for this disease over the last few years, it remains a significant area of unmet need for patients around the world. One important element of the CARDIO-TTRansform trial is that patients with ATTR cardiomyopathy will be able to continue with approved treatments as we assess AKCEA-TTR-L_{Rx}. We have the potential to bring a new range of treatment options to patients living with both the hereditary and wild type forms of this fatal disease," said Stephen Heitner, M.D., associate professor of medicine at Oregon Health and Science University.

CARDIO-TTRansform Phase 3 Study Design:

CARDIO-TTRansform is a global, double-blind, randomized, placebo-controlled Phase 3 cardiovascular outcome study. It is designed to compare AKCEA-TTR-L_{Rx} to placebo in patients with both wild type and hereditary ATTR cardiomyopathy who are on the current available standard of care. The primary composite endpoint is cardiovascular (CV) mortality and frequency of CV clinical events comparing the two study arms at Week 120. Secondary endpoints include the change from baseline in the 6-minute walk test and in the Kansas City Cardiomyopathy Questionnaire (KCCQ) scores, as well as the rates of CV mortality, CV clinical events, and all-cause mortality at Week 120.

For more information on the CARDIO-TTRansform study, please visit the CARDIO-TTRansform website at www.CARDIO-TTRansform.com or www.clinicaltrials.gov (NCT04136171).

AKCEA-TTR-L_{Rx} is also being studied in patients with polyneuropathy caused by hereditary TTR amyloidosis, or hATTR amyloidosis. For more information on the Phase 3 NEURO-TTRansform study, please visit www.NEURO-TTRansform.com or www.clinicaltrials.gov (NCT04136184).

ABOUT AKCEA-TTR-L_{Rx}

AKCEA-TTR-L_{Rx} is an antisense drug that uses Ionis' advanced **LI**gand **C**onjugated **A**ntisense, or LICA, technology. It was discovered by Ionis and is being co-developed by Ionis and Akcea. AKCEA-TTR-L_{Rx} inhibits the production of the transthyretin (TTR) protein at its source. AKCEA-TTR-L_{Rx} is in development to treat a broad population of patients with both hereditary and wild-type forms of transthyretin amyloidosis, or ATTR amyloidosis.

ABOUT IONIS PHARMACEUTICALS, INC.

As the leader in RNA-targeted drug discovery and development, Ionis has created an efficient, broadly applicable, drug discovery platform called antisense technology that can 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. We created the first and only approved treatment for children and adults with spinal muscular atrophy as well as the world's first RNA-targeted therapeutic approved for the treatment of polyneuropathy in adults with hereditary transthyretin amyloidosis. Our sights are set on all the patients we have yet to reach with a pipeline of more than 40 novel medicines designed to treat a broad range of diseases including cardiovascular diseases, neurological diseases, infectious diseases, pulmonary diseases and cancer.

To learn more about Ionis visit www.ionispharma.com and follow us on Twitter @ionispharma.

ABOUT AKCEA THERAPEUTICS

Akcea Therapeutics, Inc., a majority-owned affiliate of Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), is a biopharmaceutical company focused on developing and commercializing drugs to treat patients with serious and rare diseases. Akcea is commercializing TEGSEDI® (inotersen) and WAYLIVRA® (volanesorsen), as well as advancing a mature pipeline of novel drugs, including AKCEA-APO(a)-L_{Rx}, AKCEA-ANGPTL3-L_{Rx}, AKCEA-APOCIII-L_{Rx}, and AKCEA-TTR-L_{Rx}, with the potential to treat multiple diseases. All six drugs were discovered by 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 approved in the E.U. 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 and you can follow us on Twitter at @akceatx.

AKCEA AND IONIS FORWARD-LOOKING STATEMENT

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-TTR-L_{Rx}. Any statement describing Akcea's or Ionis' goals, expectations, financial or other projections, intentions or beliefs, including the commercial potential of AKCEA-TTR-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 Akcea's and Ionis' programs are described in additional detail in Akcea's and Ionis' 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.

For More Information:

Akcea Investor Contact:
Kathleen Gallagher
Vice President of Communications and Investor Relations
(617)-207-8509
kgallagher@akceatx.com

Akcea Media Contact:
Lynn Granito
Berry & Company
T: 212 253-8881
lgranito@berrypr.com

Ionis Investor Contact:
D. Wade Walke, Ph.D.
Vice President, Investor Relations
760-603-2741
wwalke@ionisph.com

Ionis Media Contact:
Roslyn Patterson
Vice President, Corporate Communications
760-603-2681
rpatterson@ionisph.com

Source: Akcea Therapeutics, Inc.