Positive Phase 1 Results of AKCEA-TTR-LRx Presented at the Heart Failure Society of America Annual Meeting

September 16, 2019

Data show >90% knockdown of TTR following administration in healthy volunteers

Positive safety and tolerability profile for LICA platform-based therapy

Phase 3 program on track to start later this year in patients with all forms of TTR amyloidosis

BOSTON and CARLSBAD, Calif., Sept. 16, 2019 (GLOBE NEWSWIRE) -- Akcea Therapeutics, Inc. (NASDAQ: AKCA), an affiliate of Ionis Pharmaceuticals, Inc., and Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), presented data today from the Phase 1 clinical trial of AKCEA-TTR-L_{Rx} in a poster presentation at the Heart Failure Society of America 23rd Annual Scientific Meeting in Philadelphia, Pennsylvania.

AKCEA-TTR-L_{Rx} is an antisense drug developed using Ionis' proprietary **LI**gand **C**onjugated **A**ntisense (LICA) technology platform. It was discovered by Ionis and is being co-developed by Ionis and Akcea. AKCEA-TTR-L_{Rx} is designed to inhibit the production of transthyretin, or TTR, and is being studied in patients with both the hereditary and the wild type forms of TTR amyloidosis or ATTR.

AKCEA-TTR-L_{Rx} Phase 1 Study Results:
The goal of the Phase 1 study was to assess the effects of AKCEA-TTR-L_{Rx} on TTR levels in healthy volunteers. In the randomized, double-blind, placebo-controlled, dose-escalation study healthy volunteers were administered AKCEA-TTR-L_{Rx} or placebo via a single subcutaneous injection or once every four weeks for 13 weeks followed by an additional 13-week period where patients did not receive treatment. Results from the Phase 1 study show:

- Patients who received injections of 45mg monthly achieved a mean reduction in TTR levels of 86% at Week 13.
- Patients who received injections of 90mg monthly achieved a mean reduction in TTR levels of 94% at Week 13.
- Patients who received a single 120mg injection achieved a mean TTR reduction of 86% at Week 4.
- All adverse events (AEs) were mild with the exception of one moderate AE (headache).
- No AEs led to an interruption in dosing.
- There were no severe adverse events in patients treated with AKCEA-TTR-L_{Rx}.

Akcea and Ionis also plan to initiate the Phase 3 program for AKCEA-TTR-L_{Rx} later this year.

"The Phase 1 data demonstrate an impressive and meaningful reduction in the TTR protein while maintaining a positive safety and tolerability profile with monthly administration of AKCEA-TTR-L_{Rx}. These results are encouraging as we expand our commitment to the TTR amyloidosis community through development of AKCEA-TTR-L_{Rx} for patients with both hereditary and wild type forms of ATTR amyloidosis," said Louis O'Dea, chief medical officer at Akcea Therapeutics. "Our goal is to improve patients' lives with a safe and efficacious therapy that targets and reduces TTR protein at its source. The convenience of monthly administration would also represent a significant advantage for patients living with this debilitating and fatal disease."

"The significant reductions in TTR levels following treatment combined with a positive safety and tolerability profile further validate the potential of our LICA technology platform to deliver important treatments to patients who are in need of therapeutic options," said Brett P. Monia, Ph.D., chief operating officer of Ionis Pharmaceuticals. "These data are consistent with the clinical profile seen across our other LICA programs and demonstrate how this advancement in our technology positions us to address more common diseases, including ATTR cardiomyopathy. We look forward to continuing to make important progress in our LICA platform and to advancing the AKCEA-TTR-L_{Rx} program through Phase 3."

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. AKCEA-TTR-L_{Rx} is currently in a Phase 1/2 study with initiation of the Phase 3 program planned for later in 2019.

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, 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 commercializing TEGSEDI® (inotersen) and advancing a mature pipeline of novel drugs, including WAYLIVRA® (volanesorsen), 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.

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