Akcea and Ionis Announce Initiation of NEURO-TTRansform Phase 3 Clinical Trial for AKCEA-TTR-LRx in Patients with Polyneuropathy Driven by Hereditary TTR Amyloidosis

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BOSTON and CARLSBAD, Calif., Nov. 25, 2019 (GLOBE NEWSWIRE) -- Akcea Therapeutics, Inc. (NASDAQ: AKCA), a majority-owned affiliate of Ionis Pharmaceuticals, Inc., and Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), today announced initiation of the NEURO-TTRansform Phase 3 clinical trial for AKCEA-TTR-L_{Rx} in patients with polyneuropathy caused by hereditary TTR amyloidosis, or hATTR amyloidosis.

“The initiation of the TTRansform Phase 3 program represents an expansion of our dedication and commitment to the ATTR community. The NEURO-TTRansform study is the first of two Phase 3 studies that we expect to initiate with AKCEA-TTR-L_{Rx}. Our Phase 1 data are encouraging and we are excited about the possibility of delivering a significant advancement for people living with hATTR amyloidosis,” said Damien McDevitt, Ph.D., interim chief executive officer at Akcea.

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.

“The Phase 1 data of AKCEA-TTR-L_{Rx} are consistent with the clinical profile seen across our other LICA programs, highlighting the potential of LICA-engineered therapies to address both rare and more common diseases,” said Brett P. Monia, Ph.D., chief operating officer of Ionis. “We remain dedicated to advancing this important clinical development program as rapidly as possible and are hopeful about the prospect of bringing a new safe and effective treatment to people living with the devastating symptoms of hATTR amyloidosis in the years ahead.”

NEURO-TTRansform Phase 3 Study Design

NEURO-TTRansform is a global, open-label, randomized study evaluating the efficacy and safety of AKCEA-TTR-L_{Rx} in patients with polyneuropathy due to hATTR amyloidosis. The study will enroll 140 adult patients with stage 1 or stage 2 polyneuropathy and will be compared to the historical placebo arm from the TEGSEDI® (inotersen) NEURO-TTR Phase 3 study that was completed in 2017. Of the total 140 participants, 20 patients will begin on TEGSEDI and move to AKCEA-TTR-L_{Rx} after week 35. The primary endpoint analysis will be completed at week 66 and all patients will be followed until week 85 when they will have the option to transition into the open label extension study.

The co-primary efficacy endpoints at week 66 are:

- Percent change from baseline in serum TTR concentration;
- Change from baseline in the modified Neuropathy Impairment Score +7 (mNIS+7), a measure of neuropathic disease progression; and
- Change from baseline in Norfolk Quality of Life Questionnaire-Diabetic Neuropathy (Norfolk QoL-DN).

There will be an interim analysis at week 35 where the co-primary efficacy endpoints are percent change from baseline in serum TTR concentration and change from baseline in mNIS+7.

For more information on the NEURO-TTRansform study, please visit www.clinicaltrials.gov.

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 HEREDITARY TRANSTHYRETIN (hATTR) AMYLOIDOSIS

hATTR amyloidosis is a severe, progressive, and life-threatening disease caused by the abnormal formation of the TTR protein and aggregation of TTR amyloid deposits in various tissues and organs throughout the body, including in peripheral nerves, the heart and intestinal tract. The progressive accumulation of TTR amyloid deposits in these organs often leads to intractable peripheral sensorimotor neuropathy, autonomic neuropathy, and/or cardiomyopathy, as well as other disease manifestations. hATTR amyloidosis causes significant morbidity and progressive decline in quality of life, severely impacting activities of daily living. The disease often progresses rapidly and can lead to premature death. The median survival is 4.7 years following diagnosis. Additional information on hATTR amyloidosis, including a full list of organizations supporting the hATTR amyloidosis community worldwide, is available at www.hattrchangethecourse.com or by visiting www.hATTRGuide.com.

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.

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