



Akcea Retains Rights to AKCEA-APOCIII-LRx

December 18, 2019

Data from Phase 2 clinical trial of AKCEA-APOCIII-LRx anticipated in early 2020

BOSTON and CARLSBAD, Calif., Dec. 18, 2019 (GLOBE NEWSWIRE) -- Akcea Therapeutics, Inc. (NASDAQ: AKCA), a majority-owned affiliate of Ionis Pharmaceuticals, Inc., and Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), today announced that, following a strategic portfolio decision by Novartis not to exercise its option, Akcea has retained rights to develop and commercialize AKCEA-APOCIII-LRx.



"AKCEA-APOCIII-LRx has advanced rapidly in the past year and we are excited to drive the development and commercial strategy for this drug. We plan to focus our efforts on developing AKCEA-APOCIII-LRx for familial chylomicronemia syndrome, or FCS, plus other indications that could be positively impacted by reducing APOCIII and triglycerides. We look forward to seeing the results from our Phase 2 study of AKCEA-APOCIII-LRx early in 2020," said Damien McDevitt, Ph.D., interim chief executive officer at Akcea. "Novartis remains a strategic partner for Akcea. Novartis has made AKCEA-APO(a)-LRx, also known as TQJ230, a key priority in its pipeline and has already begun the Lp(a)HORIZON Phase 3 cardiovascular outcomes study."

AKCEA-APOCIII-LRx was discovered by Ionis and is being co-developed by Akcea and Ionis. It is an antisense drug developed using Ionis' advanced **L**igand **C**onjugated **A**ntisense (LICA) technology platform. It is designed to reduce the production of apolipoprotein C-III, or apoC-III, which is potentially a key target for addressing multiple diseases including FCS and cardiovascular disease, or CVD. AKCEA-APOCIII-LRx is currently in Phase 2 clinical development to treat patients with hypertriglyceridemia and CVD. Akcea and Ionis remain on track to announce topline results from this Phase 2 clinical study in early 2020.

ABOUT AKCEA-APOCIII-LRx

AKCEA-APOCIII-LRx is a ligand conjugated antisense (LICA) drug designed to reduce the production of apolipoprotein C-III, or apoC-III. ApoC-III is a protein produced in the liver that plays a central role in the regulation of serum triglycerides. Genetically reduced levels of apoC-III are correlated to lower levels of triglycerides and lower risk of cardiovascular disease whereas elevated levels of apoC-III correlate with high triglyceride levels that have been associated with multiple metabolic abnormalities, such as insulin resistance and/or metabolic syndrome. Akcea and Ionis are developing AKCEA-APOCIII-LRx to treat hypertriglyceridemia and established cardiovascular disease with data anticipated from the Phase 2 program early in 2020.

Results from a Phase 1/2 clinical trial of AKCEA-APOCIII-LRx showed significant, dose-dependent reductions in apoC-III protein of up to 84 percent after six weeks of treatment and in triglyceride levels of up to 71 percent. Significant dose-dependent reductions of up to 30% in apolipoprotein B (apoB) and increases of up to 100% in high-density lipoprotein cholesterol (HDL-C) were also observed. Both decreased levels of apoB and increased levels of HDL-C are associated with decreased cardiovascular risk. In the Phase 1/2 study there were no serious adverse events or adverse events leading to treatment discontinuation. There were no hepatic or renal signals, injection site or flu-like reactions and no clinically significant findings in routine hematology or biochemistry, including no platelet reductions.

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-APOCIII-L_{Rx} and AKCEA-APO(a)-L_{Rx}. Any statement describing Akcea's or Ionis' goals, expectations, financial or other projections, intentions or beliefs, including the commercial potential of AKCEA-APOCIII-L_{Rx}, AKCEA-APO(a)-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.

Ionis Pharmaceuticals™ is a trademark of Ionis Pharmaceuticals, Inc. Akcea Therapeutic®, TEGSEDI® and WAYLIVRA® are trademarks of Akcea Therapeutics, Inc.

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

