Akcea and Ionis report top-line results from the BROADEN Study with WAYLIVRA® (volanesorsen) in patients with familial partial lipodystrophy

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Study meets primary and key secondary endpoints

BOSTON, Mass. and CARLSBAD, Calif., Aug. 06, 2019 (GLOBE NEWSWIRE) -- Akcea Therapeutics, Inc. (NASDAQ: AKCA), an affiliate of Ionis Pharmaceuticals, Inc., and Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), announced today topline results from the BROADEN study in patients with familial partial lipodystrophy (FPL). The study met its primary endpoint demonstrating a statistically significant reduction in triglyceride levels in patients with FPL treated with WAYLIVRA compared to placebo-treated patients. In addition to achieving the primary endpoint, the study achieved an important secondary endpoint of a statistically significant reduction in liver fat.

“We are encouraged by the substantial reduction in triglycerides and hepatic fat fraction achieved with WAYLIVRA in patients with FPL and we will be reviewing the totality of the data internally and with experts in the field to determine the most appropriate next steps for this program,” said Louis O’Dea, chief medical officer at Akcea Therapeutics. “We are grateful to the FPL patient community for their input and participation, and we understand their desperate need for a treatment option.”

“We are pleased by the safety and efficacy profile demonstrated by WAYLIVRA in patients with FPL, adding to the already established profile in patients with FCS,” said Brett P. Monia, Ph.D., chief operating officer of Ionis Pharmaceuticals. “These results represent another important outcome of our antisense platform for patients desperate for new treatment options.”

Akcea and Ionis received marketing authorization in Europe for WAYLIVRA in May 2019 as an adjunct to diet in adult patients with genetically confirmed FCS and at high risk for pancreatitis, in whom response to diet and triglyceride lowering therapy has been inadequate. The Companies’ efforts are focused on the commercial launch of WAYLIVRA in the EU and working with regulatory agencies to determine a path forward so that patients with FCS in the U.S. and Canada may have access to this treatment.

BROADEN Study Background and Results:
The goal of the BROADEN study was to assess the effects of WAYLIVRA on triglyceride levels and other metabolic parameters in people with FPL, a rare lipid disorder characterized by metabolic abnormalities, including hypertriglyceridemia, elevated liver fat, extreme insulin resistance and abnormalities in the distribution of body fat. The randomized, placebo-controlled, double-blind study included 40 patients (≥18 years old) with a clinical diagnosis of FPL plus hypertriglyceridemia and fatty liver. Participants were administered WAYLIVRA or placebo via subcutaneous injection. Results from the study show:

- A statistically significant mean reduction from baseline of 88% in triglyceride levels in WAYLIVRA-treated patients at 3 months compared to 22% reduction in placebo-treated patients (primary endpoint, $p<0.001$). Significant triglyceride lowering was maintained throughout the 12 months study period.
- A statistically significant mean reduction from baseline of 51.9% in liver fat in WAYLIVRA-treated patients at 12 months compared to a 1.5% increase in placebo-treated patients ($p=0.004$).

The most common adverse events observed in WAYLIVRA-treated patients were mild or moderate in severity and included injection site reactions, nasopharyngitis, urinary tract infection and reductions in platelet levels. There were no serious or severe decreases in platelets.

About FPL
Familial Partial Lipodystrophy, or FPL, is a rare lipid disorder characterized by abnormal fat distribution across the body and a range of metabolic abnormalities, including severe insulin resistance, dyslipidemia and hypertriglyceridemia, hepatic steatosis and, in affected women, features of hyperandrogenism. People with FPL often present with polycystic ovarian syndrome or unusually insulin-resistant diabetes and are at increased risk of acute pancreatitis in addition to long-term, progressive consequences including premature cardiovascular disease and liver disease, resulting in cirrhosis. They are unable to store fat or triglycerides in normal fat stores, so excess triglycerides are stored in the liver and muscle and accumulate at high levels in the bloodstream. Additional information on FPL is available through Lipodystrophy United at www.lipodystrophyunited.org.

About WAYLIVRA® (volanesorsen) for the treatment of FCS
WAYLIVRA, which received marketing authorization in Europe in May 2019, is the only therapy indicated for people with familial chylomicronemia syndrome (FCS). Akcea and Ionis are working to confirm a path forward for WAYLIVRA in the U.S. and Canada.

WAYLIVRA, a product of Ionis' proprietary antisense technology, is designed to reduce the production of ApoC-III, a protein that regulates plasma triglycerides and may also affect other metabolic parameters.

The European Commission's marketing authorization of WAYLIVRA is based on results from the Phase 3 APPROACH study and the ongoing APPROACH Open Label Extension (OLE) study and is supported by results from the Phase 3 COMPASS study. Results from the Phase 3 APPROACH trial, the largest study ever conducted in patients with FCS, show that in comparison to placebo, treatment with WAYLIVRA reduced triglycerides 77% (-94% when compared to placebo). All patients in the trial maintained a low-fat diet.

WAYLIVRA is associated with risk of thrombocytopenia. Enhanced monitoring is required to support early detection and management of thrombocytopenia. The most frequently observed adverse reactions (more than 10%) during treatment with WAYLIVRA were events associated with injection site reactions and reduction in platelet levels/thrombocytopenia.

Click here for more information on the WAYLIVRA Early Access Program, or EAP. For more information on WAYLIVRA, please visit www.WAYLIVRA.eu.

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 and co-developed with 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'S 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 WAYLIVRA® (volanesorsen) and other products in development. Any statement describing Ionis' or Akcea's goals, expectations, financial or other projections, intentions or beliefs, including the commercial potential of WAYLIVRA 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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