



Akcea and Ionis receive positive EU CHMP opinion for WAYLIVRA (volanesorsen)

March 1, 2019

First and only therapy approved for FCS, a serious and rare disease with no approved treatment options

BOSTON, Mass. and CARLSBAD, Calif., March 01, 2019 (GLOBE NEWSWIRE) -- Akcea Therapeutics, Inc. (NASDAQ: AKCA), an affiliate of Ionis Pharmaceuticals, Inc., and Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion recommending conditional marketing authorization for WAYLIVRA as an adjunct to diet in adult patients with genetically confirmed familial chylomicronemia syndrome (FCS) who are at high risk for pancreatitis, in whom response to diet and triglyceride lowering therapy has been inadequate. [Click here](#) to read the EMA's press release.



The positive opinion will now be referred to the European Commission (EC), which grants marketing authorization for medicines in the European Union for the adoption of a decision on an EU-wide marketing authorization. As part of the conditional marketing authorization, Akcea and Ionis will conduct a non-interventional post-authorization safety study (PASS) based on a Registry.

"This positive CHMP opinion is an important step forward as we work to bring WAYLIVRA to people living with FCS who currently have no treatment options. Once approved, WAYLIVRA will be the first and only therapy for people living with the devastating challenges of FCS. We are now anticipating approval in Europe in the coming months. We will build on the strong infrastructure we have in place for TEGSEDI® (inotersen) in Europe as we prepare for the launch of WAYLIVRA," said Paula Soteropoulos, chief executive officer of Akcea Therapeutics. "This is a testament to the European Regulatory Authorities' commitment to facilitating access to innovative medicines for patients in need."

WAYLIVRA's Marketing Authorization Application (MAA) is based on results from the Phase 3 APPROACH study and the ongoing APPROACH Open Label Extension study and 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 by 77 percent after 3 months of treatment. The most common adverse events in the APPROACH study were injection site reactions and reductions in platelet levels. In addition to the OLE study, there are also ongoing global Early Access Programs for WAYLIVRA.

"The FCS community is encouraged by the positive CHMP opinion and we remain very hopeful that people living with FCS will soon have an approved treatment available in the EU," said Jill Praver, founder and chair, LPLD Alliance "Without a treatment, people living with FCS have debilitating daily symptoms as well as the constant fear of pancreatitis. This is a positive step forward for people living with FCS who currently have no treatment options. Patients around the world need and deserve a treatment for FCS."

"WAYLIVRA will be the third medicine for which we will have received approval in the last two years. Our antisense technology platform continues to deliver many important scientific and medical advances that should support continuing growth," said Brett P. Monia, Ph.D., chief operating officer of Ionis Pharmaceuticals. "We look forward to continuing to work with the community of patients and the dedicated clinicians and researchers around the world to make this treatment available to patients who need it as

quickly as possible.”

ABOUT WAYLIVRA AND FCS

WAYLIVRA, a product of Ionis' proprietary antisense technology, is designed to reduce the production of ApoC-III, a protein produced in the liver that plays a central role in the regulation of plasma triglycerides and may also affect other metabolic parameters.

WAYLIVRA is under regulatory review in the E.U. for the treatment of people with familial chylomicronemia syndrome (FCS). Akcea is working to confirm a path forward for WAYLIVRA in the US and in Canada.

FCS is an ultra-rare disease caused by impaired function of the enzyme lipoprotein lipase (LPL) and characterized by severe hypertriglyceridemia (>880mg/dL) and a risk of unpredictable and potentially fatal acute pancreatitis. Because of limited LPL function, people with FCS cannot breakdown chylomicrons, lipoprotein particles that are 90% triglycerides. In addition to pancreatitis, FCS patients are at risk of chronic complications due to permanent organ damage, including chronic pancreatitis and pancreatogenic diabetes. They can experience daily symptoms including abdominal pain, generalized fatigue and impaired cognitions that affect their ability to work. People with FCS also report major emotional and psychosocial effects including anxiety, social withdrawal, depression and brain fog. There is no effective therapy for FCS currently available. Additional information on FCS is available at www.fcsfocus.com, through the LPLD Alliance at www.lpldalliance.org and through the FCS Foundation at <http://www.livingwithfcs.org>. For a full list of organizations supporting the FCS community worldwide, please click [here](#).

WAYLIVRA is also currently in Phase 3 clinical development for the treatment of patients with familial partial lipodystrophy, or FPL. Akcea anticipates reporting top-line data from this study in mid-2019.

ABOUT AKCEA THERAPEUTICS

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)-_{Rx}, AKCEA-ANGPTL3-_{Rx}, AKCEA-APOCIII-_{Rx}, and AKCEA-TTR-_{Rx}, all with the potential to treat multiple diseases. All six drugs were discovered by and are being 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 under regulatory review for the treatment of familial chylomicronemia syndrome, or FCS, 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.

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 follow us on twitter @ionispharma or visit <http://ir.ionispharma.com/>.

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). Any statement describing Akcea's or Ionis' 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 Ionis' and Akcea's programs are described in additional detail

in Ionis' and Akcea's 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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