

Akcea and Ionis Announce Approval of WAYLIVRA® (volanesorsen) in the European Union **WAYLIVRA is the only therapy for Familial Chylomicronemia Syndrome, or FCS, a devastating, ultra-rare disease**

BOSTON and CARLSBAD, Calif., May 07, 2019 (GLOBE NEWSWIRE) -- Akcea Therapeutics, Inc. (NASDAQ:AKCA), an affiliate of Ionis Pharmaceuticals, Inc., and Ionis Pharmaceuticals, Inc. (NASDAQ:IONS), announced today that WAYLIVRA has received conditional marketing authorization from the European Commission (EC) 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.

This authorization follows the positive opinion recommending approval provided by the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA). [Click here](#) to view the EC's decision. As part of the conditional marketing authorization, Akcea and Ionis will conduct a non-interventional post-authorization safety study (PASS) based on a Registry.

“WAYLIVRA is the only approved treatment for people with FCS and is a major milestone for the global FCS community. This also marks Akcea's second drug approval in the last year. We are very grateful to all the patients and physicians around the world who participated in our clinical trials. Their insights about the challenges of this devastating disease and their stories of how they have benefited from WAYLIVRA continue to motivate us,” said Paula Soteropoulos, chief executive officer of Akcea Therapeutics. “We plan to launch WAYLIVRA in Germany this year followed by additional European countries in 2020. Our team is ready to deliver this treatment option to patients with FCS.”

FCS is an ultra-rare debilitating disease that can be life-altering. It is caused by impaired function of the enzyme, lipoprotein lipase (LPL), which results in significant risk and disease burden, including unpredictable and potentially fatal acute pancreatitis as well as chronic complications due to permanent organ damage. It is estimated that there are between 3,000 to 5,000 people living with FCS worldwide, with approximately 1,000 people living with FCS in Europe.

“WAYLIVRA is the only treatment available for patients with FCS which makes this approval a landmark event for the global FCS community. Patients, their caretakers and their families have been suffering without any therapeutic option. Now patients across Europe can access a medicine that may help address their severely elevated triglycerides which can give them hope for better health. High triglycerides can lead to a multitude of severe and daily chronic symptoms such as abdominal pain and increased risk of pancreatitis which have a significant daily impact on people living with FCS,” said Jules Payne, chief executive at HEART UK and chair of FH Europe.

WAYLIVRA is an antisense oligonucleotide drug designed by Ionis and co-developed by Akcea and Ionis to reduce the production of ApoC-III, a protein that regulates plasma triglycerides. WAYLIVRA is a self-administered, subcutaneous injection in a single-use, prefilled syringe.

“The approval of WAYLIVRA is truly an important moment for people affected by FCS and for all of us in medicine who specialize in treating lipid disorders,” said Dr. Eric Bruckert, head of the endocrinology and prevention of cardiovascular disease department in Pitié-Salpêtrière Hospital in Paris, France. “Many clinicians are pleased to now have a treatment option available because of the significant burden of FCS on patients and their families.”

“WAYLIVRA is Ionis' third medicine approved in just over two years. Our highly efficient and productive antisense technology has the potential to treat the untreatable by precisely targeting the root cause of disease. FCS is an example of a disease that our novel technology is ideally suited to address,” said Brett P. Monia, chief operating officer at Ionis. “We are confident that our affiliate, Akcea, has built an expert team that is committed and ready to deliver WAYLIVRA to patients as soon as possible.”

The EC's marketing authorization of WAYLIVRA is based on results from the Phase 3 APPROACH study and the ongoing APPROACH Open Label Extension study and is supported by results from the Phase 3 COMPASS study. Results from the APPROACH trial, the largest study ever conducted in patients with FCS, show that in comparison to placebo treatment with WAYLIVRA delivered clinically and statistically meaningful reduction in triglycerides over the study period. An analysis of patients with a history of recurrent pancreatitis events (≥ 2 events in the five years prior to Study Day 1) showed a significant reduction in pancreatitis attacks in WAYLIVRA-treated patients compared to placebo treated patients. The most common adverse events in the APPROACH study were injection site reactions and reductions in platelet levels. In addition to the open

label extension study, there are also ongoing global Early Access Programs for WAYLIVRA.

For important safety information for WAYLIVRA, including method of administration, special warnings, drug interactions and adverse drug reactions, please see the European Summary of Product Characteristics (SmPC), which will be available on the EMA website at www.ema.europa.eu.

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

About WAYLIVRA® (volanesorsen)

WAYLIVRA is the only therapy indicated for people with familial chylomicronemia syndrome (FCS). Akcea is 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.

The WAYLIVRA Early Access Program (EAP) has been initiated in Europe, the U.S. and Canada and is currently enrolling eligible patients. [Click here](#) for more information on the WAYLIVRA EAP. For more information on WAYLIVRA, please visit www.WAYLIVRA.eu.

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 FCS

FCS is an ultra-rare disease caused by impaired function of the enzyme lipoprotein lipase (LPL) and characterized by severe hypertriglyceridemia (>880mg/dL or 10mmol/L) 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. 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](#).

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 www.ionispharma.com.

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)-LRx, AKCEA-ANGPTL3-LRx, AKCEA-APOCIII-LRx, and AKCEA-TTR-LRx, 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 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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