



## FDA Advisory Committee Votes in Favor of WAYLIVRA for Treatment of Familial Chylomicronemia Syndrome

May 10, 2018

### Advisory Committee members vote 12-8 to support approval

CAMBRIDGE, Mass. and CARLSBAD, Calif., May 10, 2018 (GLOBE NEWSWIRE) -- Akcea Therapeutics, Inc. (NASDAQ:AKCA), an affiliate of Ionis Pharmaceuticals, Inc., and Ionis Pharmaceuticals, Inc. (NASDAQ:IONS) today announced that the U.S. Food and Drug Administration's (FDA) Division of Metabolism and Endocrinology Products Advisory Committee voted 12-8 to support approval of WAYLIVRA™ (volanesorsen) for the treatment of people with familial chylomicronemia syndrome (FCS). The committee's non-binding recommendation will be considered by the FDA in its review of Akcea's New Drug Application for WAYLIVRA. The PDUFA date for completion of the review of WAYLIVRA is August 30, 2018.

"We thank the committee members for their time and their comments today. The Committee's majority vote in favor of approval is an important positive step to bring WAYLIVRA to people with FCS who have no adequate treatment options," said Paula Soteropoulos, chief executive officer of Akcea Therapeutics. "We look forward to working with the FDA to complete the final stages of regulatory review for WAYLIVRA. We are committed to the FCS community and will continue to focus on bringing WAYLIVRA, potentially the first and only treatment, to people living with this serious and potentially fatal disease."

"Given the severity of FCS and the burden it places on patients, the need for a therapy is critical. The progress in development of a potential first-ever treatment is very encouraging. The planned efforts in monitoring and education are designed to achieve the highest levels of patient adherence, compliance and safety," said Dr. Seth Baum, president, American Society for Preventive Cardiology. "The medical community is eager to have a medicine to treat our patients with FCS."

The Advisory Committee reviewed data from two Phase 3 clinical trials, APPROACH and COMPASS, as well as the ongoing APPROACH Open Label study for WAYLIVRA. Results from the phase 3 APPROACH trial, the largest study ever conducted in patients with FCS, show that patients with FCS treated with WAYLIVRA achieved a statistically significant mean reduction in triglycerides of 77% from baseline and decreased risk of pancreatitis. The most common adverse events in the APPROACH study were injection site reactions and platelet declines. The Committee's input will be considered by the FDA in its review of the New Drug Application for WAYLIVRA. The FDA is not bound by the Committee's guidance, but takes its advice into consideration when reviewing investigational medicines. WAYLIVRA is also under regulatory review in the European Union and Canada.

"People with FCS have severely elevated triglycerides, which lead to multiple severe daily and chronic symptoms, such as abdominal pain and increased risk for pancreatitis, which can be fatal. WAYLIVRA is the first drug to demonstrate substantial triglyceride lowering in clinical trials in people with FCS," said Brett P. Monia, chief operating officer at Ionis. "WAYLIVRA illustrates how our antisense technology can create targeted drugs for people living with severe diseases who currently have no available therapeutic options."

#### ABOUT WAYLIVRA AND FCS

WAYLIVRA, a product of Ionis' proprietary antisense technology, is under regulatory review in the U.S., EU and Canada as a treatment for familial chylomicronemia syndrome (FCS). The U.S. and EU regulatory agencies have granted Orphan Drug Designation to WAYLIVRA for the treatment of FCS. If approved, WAYLIVRA would be the first and only therapy indicated for people with FCS.

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. 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](http://www.fcsfocus.com), and through the FCS Foundation at <http://www.livingwithfcs.org> and the LPLD Alliance at [www.lpldalliance.org](http://www.lpldalliance.org). For a full list of organizations supporting the FCS community worldwide, please click [here](#).

WAYLIVRA 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. It 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 2019.

#### ABOUT IONIS PHARMACEUTICALS, INC.

Ionis is the leading company in RNA-targeted drug discovery and development focused on developing drugs for patients who have the highest unmet medical needs, such as those patients with severe and rare diseases. Using its proprietary antisense technology, Ionis has created a large pipeline of first-in-class or best-in-class drugs, with over 40 drugs in development. SPINRAZA® (nusinersen) has been approved in global markets for the treatment of spinal muscular atrophy (SMA). Biogen is responsible for commercializing SPINRAZA. TEGSEDI™ (inotersen) and WAYLIVRA™ (volanesorsen) are two antisense drugs that Ionis discovered and successfully advanced through Phase 3 studies. TEGSEDI is under regulatory review for marketing approval in the U.S., EU and Canada for the treatment of patients with hereditary ATTR amyloidosis, or hATTR. WAYLIVRA is under regulatory review for marketing approval in the U.S., EU, and Canada for the treatment of patients with familial chylomicronemia syndrome, or FCS. WAYLIVRA is also in a Phase 3 study in patients with familial partial lipodystrophy, or FPL. Akcea Therapeutics, an affiliate of Ionis focused on developing and commercializing drugs to treat patients with serious and rare diseases, will commercialize TEGSEDI and WAYLIVRA, if approved. Ionis' patents provide strong and extensive protection for its drugs and technology. Additional information about Ionis is available at [www.ionispharma.com](http://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 advancing a mature pipeline of six novel drugs, including TEGSEDI™ (inotersen), WAYLIVRA™ (volanesorsen), AKCEA-APO(a)-LR<sub>x</sub>, AKCEA-ANGPTL3-LR<sub>x</sub>, AKCEA-APOCIII-LR<sub>x</sub>, and AKCEA-TTR-LR<sub>x</sub>, 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 under regulatory review in the U.S., EU and Canada for the treatment of people with hereditary transthyretin amyloidosis (hATTR). WAYLIVRA is under regulatory review in the U.S., EU and Canada 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 Cambridge, Massachusetts. Additional information about Akcea is available at [www.akceatx.com](http://www.akceatx.com).

## **IONIS' AND AKCEA'S 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 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 TEGSEDI, WAYLIVRA or other of Ionis' or Akcea's 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. Ionis' and Akcea's 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 Ionis' and Akcea's forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Ionis and Akcea. 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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