



Akcea Therapeutics Receives Orphan Drug Designation from the US FDA for Volanesorsen (ISIS-APOCIII Rx) for the Treatment of Familial Chylomicronemia Syndrome

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BOSTON, July 6, 2015 /PRNewswire/ -- Akcea Therapeutics, a wholly-owned subsidiary of Isis Pharmaceuticals, Inc. (NASDAQ: ISIS), announced today that the U.S. Food and Drug Administration has granted Orphan Drug Designation to volanesorsen (ISIS-APOCIII_{Rx}) for the treatment of patients with Familial Chylomicronemia Syndrome (FCS). FCS is a rare genetic disease characterized by extremely high triglyceride levels and risk of pancreatitis. In a Phase 2 study published in the NEJM in December 2014, patients with FCS treated with volanesorsen achieved substantial reductions in apoC-III, triglycerides, chylomicrons and apoC-III-associated very low density lipoprotein-cholesterol (VLDL-C) particles.¹ Akcea is currently conducting an international multi-center, randomized, double-blind, placebo-controlled Phase 3 study in patients with FCS.



A subsidiary of Isis Pharmaceuticals, Inc.

"FCS is a rare and very serious genetic disorder associated with very high triglyceride levels that put patients at risk of potentially life-threatening pancreatitis. People with FCS cope with daily consequences of their disease, including persistent abdominal pain and life-altering food restrictions. Unfortunately, current treatment options do not reduce triglyceride levels enough to reduce the risk of serious illness in patients with FCS," said Paula Soteropoulos, President and Chief Executive Officer at Akcea Therapeutics. "Orphan drug designation for FCS underscores the need for improved therapies to treat patients with FCS and is an important benchmark as we complete the ongoing Phase 3 study in patients with FCS and prepare for commercialization."

The Orphan Drug Act provides for economic incentives to encourage the development of drugs for diseases affecting fewer than 200,000 people in the United States. Orphan drug designation entitles Akcea Therapeutics to seven years of market exclusivity in the United States if market approval is granted for volanesorsen for the treatment of patients with FCS. Additional incentives include tax credits related to clinical trial expenses, an exemption from the FDA-user fee, and FDA assistance in clinical trial design.

About FCS

FCS is a rare genetic disorder characterized by extremely high levels of triglycerides that affects an estimated one to two out of a million people. FCS may also be called familial chylomicronemia, Frederickson Type I hyperlipoproteinemia, familial lipoprotein lipase deficiency (LPLD), or familial hypertriglyceridemia. Some people with FCS may live with recurrent stomach pain, and a high risk or prior history of hospitalization for pancreatitis. FCS is primarily caused by mutations in genes that produce proteins involved in the clearance of particles that carry triglycerides, called chylomicrons. Patients with FCS are unable to effectively clear chylomicrons, and as such, have high levels of triglycerides, which increase their risk of pancreatitis, type 2 diabetes and other serious illnesses.

About Volanesorsen

Volanesorsen (ISIS-APOCIII_{Rx}) is an antisense drug in development intended to treat patients with severely high triglycerides either as a single agent or in combination with other triglyceride-lowering agents. Volanesorsen is designed to target apoC-III, a protein produced in the liver that plays a central role in the regulation of serum triglycerides.² Humans who do not produce apoC-III have lower levels of triglycerides and lower instances of cardiovascular disease.³ Humans with elevated levels of apoC-III have high triglycerides associated with multiple metabolic abnormalities, such as insulin resistance and/or metabolic syndrome.⁴ In addition, the prevalence of type 2 diabetes is increased in patients with elevated triglycerides.⁵ Humans with severely elevated

levels of triglycerides are at risk of many serious health conditions, including pancreatitis,⁴ which can be life-threatening and require hospitalization. Volanesorsen is currently being evaluated in a Phase 3 study in patients with FCS. A second Phase 3 study of volanesorsen is planned to begin later this year in patients with Familial Partial Lipodystrophy, another severe and rare lipid disorder. For more information about this clinical trial program, please visit www.apociii.com

ABOUT AKCEA THERAPEUTICS

Akcea Therapeutics is a development and commercialization company focused on transforming the lives of patients with serious cardiometabolic lipid disorders. Established as a wholly owned subsidiary of Isis Pharmaceuticals, Inc, Akcea has a robust portfolio of development-stage drugs covering multiple targets and disease states using advanced RNA-targeted antisense therapeutics. Akcea's drug pipeline includes novel antisense drugs designed to address a number of lipid risk factors, including LDL-C, ApoC-III, triglycerides and Lp(a). Akcea's most advanced program, volanesorsen, is in Phase 3 development to treat patients with ultra-orphan lipid disorders that are characterized by extremely high triglycerides and ApoC-III, including familial chylomicronemia syndrome and familial partial lipodystrophy. Akcea is located in Cambridge, Massachusetts. Additional information about Akcea is available at www.akceatx.com.

ABOUT ISIS PHARMACEUTICALS, INC.

Isis is exploiting its leadership position in RNA-targeted technology to discover and develop novel drugs for its product pipeline and for its partners. Isis' broad pipeline consists of 38 drugs to treat a wide variety of diseases with an emphasis on cardiovascular, metabolic, severe and rare diseases, including neurological disorders, and cancer. Isis' partner, Genzyme, is commercializing Isis' lead product, KYNAMRO®, in the United States and other countries for the treatment of patients with homozygous FH. Isis has numerous drugs in Phase 3 development in severe/rare diseases and cardiovascular diseases. These include volanesorsen, a drug Isis is developing and plans to commercialize through its wholly owned subsidiary, Akcea Therapeutics, to treat patients with familial chylomicronemia syndrome and familial partial lipodystrophy; ISIS-TTR_{Rx}, a drug Isis is developing with GSK to treat patients with the polyneuropathy and cardiomyopathy forms of TTR amyloidosis; and ISIS-SMN_{Rx}, a drug Isis is developing with Biogen to treat infants and children with spinal muscular atrophy, a severe and rare neuromuscular disease. Isis' patents provide strong and extensive protection for its drugs and technology. Additional information about Isis is available at www.isispharm.com.

FORWARD-LOOKING STATEMENT

This press release includes forward-looking statements regarding the business of Akcea Therapeutics, Inc., a subsidiary of Isis Pharmaceuticals and the therapeutic and commercial potential of Akcea's technologies and products in development, including volanesorsen, and other products in development. Any statement describing Akcea's goals, expectations, financial or other projections, intentions or beliefs 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 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 forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Isis. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Akcea's programs are described in additional detail in Akcea's parent company, Isis Pharmaceuticals, Inc.'s annual report on Form 10-K for the year ended December 31, 2014, and its most recent quarterly report on Form 10-Q, which are on file with the SEC. Copies of these and other documents are available at www.isispharm.com.

In this press release, unless the context requires otherwise, "Akcea," "Company," "we," "our," and "us" refers to Akcea Therapeutics.

Isis Pharmaceuticals® is a registered trademark of Isis Pharmaceuticals, Inc. Akcea Therapeutics™ is a trademark of Isis Pharmaceuticals, Inc. KYNAMRO® is a registered trademark of Genzyme Corporation.

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