Akcea Therapeutics Receives Orphan Designation in Europe for Volanesorsen for the Treatment of Familial Partial Lipodystrophy (FPL)

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CAMBRIDGE, Mass., July 28, 2016 /PRNewswire/ -- Akcea Therapeutics, a wholly-owned subsidiary of Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), announced today that the European Commission (EC) has designated volanesorsen as an orphan medicinal product for the treatment of familial partial lipodystrophy (FPL). FPL is a rare lipid disorder characterized by abnormal fat distribution across the body and a range of metabolic abnormalities, including severe type 2 diabetes, high triglycerides, and accumulation of fat in the liver. The EC's approval follows a positive opinion in June from the European Medicine Agency's (EMA) Committee for Orphan Medicinal Products. Volanesorsen is being developed for the treatment of two rare, genetic cardiometabolic diseases: familial chylomicronemia syndrome (FCS) and familial partial lipodystrophy.

"This marks an important milestone for both the FPL community and Akcea," according to Paula Soteropoulos, chief executive officer of Akcea. "Patients with FPL have a severe disease and currently no effective treatment options. Orphan designation for volanesorsen by the E.U. reflects the regulatory community's recognition of the tremendous disease burden and unmet medical need that challenges patients with FPL. This also marks an important step for Akcea as we advance towards regulatory review and potential commercialization of volanesorsen."

EC Orphan Designation is granted to drugs that are intended for the treatment of life threatening or chronically debilitating rare diseases where no therapeutic options either exist or are satisfactory. Rare diseases are those defined as having a prevalence of less than five in 10,000 in Europe. The designation provides sponsors with development and commercial incentives, including 10 years of market exclusivity, prioritized consultation by EMA on the development of the drug, including clinical studies, and certain exemptions from, or reductions in, regulatory fees. Last year, the U.S. Food and Drug Administration granted volanesorsen Orphan Drug Designation for the treatment of patients with FCS.

ABOUT VOLANESORSEN, FCS AND FPL
Volanesorsen 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 reduce the production of ApoC-III, a protein produced in the liver that plays a central role in the regulation of plasma triglycerides.

Volanesorsen is currently being evaluated in two Phase 3 registrational studies: APPROACH and BROADEN, and a third Phase 3 study, COMPASS, in patients with triglycerides above 500 mg/dL, designed to support global regulatory filings. APPROACH is a randomized, placebo-controlled study in patients with familial chylomicronemia syndrome (FCS). FCS is a rare, genetic disorder and may also be called familial chylomicronemia or Fredrickson Type 1 hyperlipoproteinemia, or familial lipoprotein lipase deficiency. People with FCS are unable to effectively clear lipid particles called chylomicrons. As a result, they have extremely high levels of triglycerides and are at risk of significant morbidity and mortality, including potentially life-threatening pancreatitis. Additional information on FCS is available at www.fcsfocus.com.

BROADEN is a randomized, placebo-controlled study in patients with familial partial lipodystrophy (FPL). 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.

For more information about this clinical trial program for volanesorsen, please visit www.apociii.com.

ABOUT AKCEA THERAPEUTICS
Akcea Therapeutics is focused on developing and commercializing drugs for patients with serious cardiometabolic diseases caused by lipid disorders. Established as a wholly owned subsidiary of Ionis Pharmaceuticals, Inc., Akcea has a robust portfolio of development-stage drugs covering multiple targets and disease states. The drugs in Akcea's pipeline are designed using Ionis' advanced RNA-targeted antisense technology to address a number of lipid risk factors, including, ApoC-III, triglycerides, Lp(a) and LDL-cholesterol. Akcea's most advanced program, volanesorsen, is in Phase 3 development to treat patients with either familial chylomicronemia syndrome (FCS) or familial partial lipodystrophy (FPL), two orphan lipid disorders that are characterized by extremely high triglycerides and ApoC-III. Akcea is located in Cambridge, Massachusetts. Additional information about Akcea is available at www.akceatx.com.

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 a dozen drugs in mid- to late-stage development. Drugs currently in Phase 3 development include volanesorsen, a drug Ionis is developing and plans to commercialize through its wholly owned subsidiary, Akcea Therapeutics, to treat patients with

either familial chylomicronemia syndrome or familial partial lipodystrophy; IONIS-TTR$_{Rx}$, a drug Ionis is developing with GSK to treat patients with all forms of TTR amyloidosis; and nusinersen, a drug Ionis is developing with Biogen to treat infants and children with spinal muscular atrophy. Ionis' patents provide strong and extensive protection for its drugs and technology. Additional information about Ionis is available at www.ionispharma.com.

FORWARD-LOOKING STATEMENT

This press release includes forward-looking statements regarding the business of Akcea Therapeutics, Inc., a wholly owned subsidiary of Ionis 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 Akcea. 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, Ionis Pharmaceuticals, Inc.'s annual report on Form 10-K for the year ended December 31, 2015, 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.ionispharma.com.

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

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SOURCE Ionis Pharmaceuticals, Inc.

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