



A subsidiary of Ionis Pharmaceuticals, Inc.

Ionis and Akcea Close on Strategic Collaboration with Global Pharmaceutical Company to Develop and Commercialize AKCEA-APO(a)-L_{Rx} and AKCEA-APOCIII-L_{Rx}

- Ionis and Akcea to receive \$75 million up-front payment
 - Deal valued at more than \$1 billion

CARLSBAD, Calif. and CAMBRIDGE Mass., Feb. 16, 2017 /PRNewswire/ – Ionis Pharmaceuticals, Inc. (NASDAQ: IONS) and Akcea Therapeutics, a wholly-owned subsidiary of Ionis Pharmaceuticals, Inc., announced today they have closed on their exclusive, worldwide option and collaboration agreement with Novartis to develop and commercialize AKCEA-APO(a)-L_{Rx} and AKCEA-APOCIII-L_{Rx} following clearance under the Hart-Scott-Rodino Antitrust Improvements Act. Following this approval and closing of the transaction, Novartis will pay Ionis and Akcea a \$75 million up-front payment and make a \$100 million equity investment in Ionis, which equates to 1,631,435 shares at \$61.30 per share. Novartis has an obligation to make a further equity investment of \$50 million in the next 18 months in either Ionis at the same premium as the initial investment or in Akcea. Ionis and Akcea are also eligible to receive a license fee as well as development, regulatory and commercial milestone payments for each drug as it advances. In addition, Ionis and Akcea are eligible to receive tiered royalties in the mid-teens to low twenty percent range on net sales of each drug.

ABOUT Lp(a)

Lp(a) is considered a key driver for cardiovascular disease due to its association with an increased risk of coronary heart disease. Lp(a) is a lipoprotein particle that is assembled in the liver and consists of the apolipoprotein(a) protein covalently linked to LDL-cholesterol. Diet and lifestyle changes have little impact on Lp(a) levels and current therapies are not able to adequately reduce elevated levels of Lp(a) to acceptable levels in patients who have severely elevated Lp(a). Additional information is available through Lipoprotein (a) Foundation at www.lipoproteinafoundation.org.

In a Phase 1/2a study in healthy volunteers with elevated Lipoprotein(a), AKCEA-APO(a)-L_{Rx} produced significant and sustained reductions in Lp(a) of up to 97% with mean reduction of 79% after only a single, small volume dose and with multiple doses, observed reductions of Lp(a) of up to 99% with a mean reduction of 92%.

ABOUT APOCIII AND TRIGLYCERIDES

ApoC-III is a protein produced in the liver that plays a central role in the regulation of serum triglycerides. Humans who do not produce ApoC-III have lower levels of triglycerides and lower instances of cardiovascular disease. Humans with elevated levels of ApoC-III have high triglycerides associated with multiple metabolic abnormalities, such as insulin resistance and/or metabolic syndrome. In addition, the prevalence of type 2 diabetes is increased in patients with elevated triglycerides.

AKCEA-APOCIII-L_{Rx} is currently being evaluated in a Phase 1/2a study in healthy volunteers with elevated triglycerides.

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 <http://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 three dozen drugs in development. SPINRAZA™ (nusinersen) is a drug that has been approved in the U.S. for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients. Biogen is responsible for commercialization of SPINRAZA. 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; and IONIS-TTR_{Rx}, a drug Ionis is developing with GSK to treat patients with TTR amyloidosis. Ionis' patents provide strong and extensive protection for its drugs and technology. Additional information about Ionis is available at www.ionispharma.com.

IONIS PHARMACEUTICALS' FORWARD-LOOKING STATEMENT

This press release includes forward-looking statements regarding Ionis Pharmaceuticals' business, its agreement with Novartis, and the development, activity, therapeutic and commercial potential and safety of IONIS-APO(a)-L_{Rx} and IONIS-APOCIII-L_{Rx}. Any statement describing Ionis' 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. 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 Ionis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Ionis. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Ionis' programs are described in additional detail in Ionis' 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 from the Company.

In this press release, unless the context requires otherwise, "Ionis," "Company," "we," "our," and "us" refers to Ionis Pharmaceuticals and its subsidiaries.

Ionis Pharmaceuticals™ is a trademark of Ionis Pharmaceuticals, Inc. Akcea Therapeutics™ is a trademark of Ionis Pharmaceuticals, Inc. SPINRAZA™ is a trademark of Biogen.

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