

Ionis and AstraZeneca Advance First Generation 2.5 LICA Drug into Preclinical Development to Treat Cardiovascular Disease

December 19, 2016

Ionis earns \$25 million milestone payment

CARLSBAD, Calif., Dec. 19, 2016 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS) announced today that it has advanced its lead drug candidate IONIS-AZ4-2.5-L_{RX}, which has now been renamed AZD8233, into preclinical development. AZD8233 is designed to inhibit an undisclosed target to treat cardiovascular disease and is also the first of a new class of antisense drugs that uses both Ionis' proprietary Generation 2.5 chemistry and its **L**igand **C**onjugated **A**ntisense or LICA technology. In conjunction with this milestone, Ionis earned a \$25 million milestone payment from AstraZeneca (NYSE:AZN).



"This is the first drug to enter development under our strategic collaboration with AstraZeneca in cardiovascular, metabolic and renal diseases. We are pleased with how quickly this important program has advanced. AZD8233 incorporates many of the recent advancements we have made in antisense technology, including LICA and Generation 2.5 chemistry," said Brett Monia, Ph.D., senior vice president of drug discovery at Ionis. "By combining Generation 2.5 and LICA, we have generated a drug that has the advantages of both higher affinity chemistry and efficient cell-specific targeting. This combination has allowed us to produce a drug that is substantially more potent than either Generation 2.5 or LICA alone, which should support both a very low dose and infrequent dosing."

As AZD8233 advances in development, Ionis will be eligible to receive up to \$300 million in additional development and regulatory milestone payments as well as tiered, low double-digit royalties from sales of the drug. AstraZeneca will be responsible for further developing and commercializing AZD8233.

ABOUT IONIS AND ASTRAZENECA

AstraZeneca and Ionis have a strategic alliance focused on leveraging antisense technology to discover and develop antisense therapies for cardiovascular, metabolic and renal diseases. The collaboration builds on a broad existing relationship between the two companies and is supported by Ionis' expertise in cardiovascular disease and antisense technology and AstraZeneca's drug development expertise and infrastructure. In the collaboration, Ionis is primarily responsible for creating development candidates. AstraZeneca paid Ionis an upfront fee of \$65 million at the initiation of the collaboration. Beyond AZD8233, AstraZeneca has the option to license additional antisense drugs upon development candidate nomination and will pay a license fee for each drug licensed plus development and regulatory milestones and sales royalties for each program that AstraZeneca advances. Ionis and AstraZeneca are also collaborating to discover and develop antisense drugs to treat cancer.

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 TTR amyloidosis; and SPINRAZATM (nusinersen), a drug licensed by Biogen to treat infantile and later-onset 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.

ABOUT ASTRAZENECA

AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of diseases in three main therapy areas - Oncology, Cardiovascular & Metabolic Diseases and Respiratory. The Company also is selectively active in the areas of autoimmunity, neuroscience and infection. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information, please visit www.astrazeneca.com.

IONIS PHARMACEUTICALS' FORWARD-LOOKING STATEMENT

This press release includes forward-looking statements regarding Ionis' alliance with AstraZeneca. 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.

To view the original version on PR Newswire, visit: <http://www.prnewswire.com/news-releases/ionis-and-astrazeneca-advance-first-generation-25-lica-drug-into-preclinical-development-to-treat-cardiovascular-disease-300381338.html>

SOURCE Ionis Pharmaceuticals, Inc.

Ionis Pharmaceuticals Investor and Media Contact: D. Wade Walke, Ph.D., Vice President, Corporate Communications and Investor Relations, 760-603-2741