Ionis provides update on development program evaluating PCSK9 antisense medicine for the treatment of hypercholesterolemia

September 23, 2022

- *ION449 (AZD8233) met primary endpoint in Phase 2b SOLANO study for patients with hypercholesterolemia*
- *ION449 will not advance into Phase 3 development based on pre-specified criteria*

CARLSBAD, Calif., Sept. 23, 2022 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today announced that topline results from the Phase 2b SOLANO study in patients with hypercholesterolemia demonstrated that 60mg of ION449 (AZD8233) administered monthly achieved a statistically significant 62.3% ($p<0.001$) reduction in low-density lipoprotein cholesterol (LDL-C) levels after 28 weeks compared to placebo, meeting the study's primary efficacy endpoint. ION449 was generally safe and well tolerated in this study. However, these results did not achieve pre-specified efficacy criteria and AstraZeneca has decided not to advance ION449 (AZD8233) into Phase 3 development for hypercholesterolemia. AstraZeneca is continuing to analyze the results from the SOLANO study to determine its next steps for the program.

"While the LDL-C reductions seen in high-risk hypercholesterolemia patients on maximum statin therapy were both statistically significant and robust, these results did not meet AstraZeneca's target product profile criteria to invest in a broad Phase 3 development program," said Eugene Schneider, M.D., executive vice president, chief clinical development officer at Ionis. "AstraZeneca continues to be a valued collaborator and we look forward to working with them to advance multiple important programs."

About SOLANO

SOLANO (NCT04964557) was a randomized parallel, double-blind, placebo-controlled Phase 2b study in 411 participants with hyperlipidemia LDL-C ≥70 mg/dL and <190mg/dL on maximum tolerated statin and/or ezetimibe. The primary objectives of this study were to assess the efficacy, safety and tolerability of ION449 (AZD8233) as compared with placebo.

About ION449

ION449 (AZD8233) dosed once monthly via subcutaneous administration, is an investigational medicine that uses Ionis' advanced **LI**gand-**C**onjugated **A**ntisense (LICA) technology platform. It is designed to reduce plasma levels of proprotein convertase subtilisin/kexin type 9 (PCSK9). PCSK9 is integrally involved in the regulation of LDL-cholesterol. Genetic studies have shown that individuals with life-long reduction of LDL-C due to reduced function of PCSK9 have substantially reduced risk of cardiovascular disease. Pharmacological inhibition of PCSK9 substantially lowers LDL-C. ION449 is designed to reduce the liver production of PCSK9 and lower the plasma level of LDL-C and thus reduce the risk of cardiovascular disease. AstraZeneca licensed ION449 from Ionis in 2015.

About Hypercholesterolemia

Hypercholesterolemia, or elevated LDL-C levels in the blood, is an important risk factor for cardiovascular disease, the leading cause of death worldwide. There is a significant unmet medical need for stronger LDL-C lowering therapies in secondary prevention patients with approximately 50% who are not meeting their treatment goals despite taking a high-intensity statin. It is estimated that one in six patients with LDL-C >100mg/dL will suffer a second major adverse cardiovascular event over approximately three years.

About Ionis Pharmaceuticals, Inc.

For more than 30 years, Ionis has been the leader in RNA-targeted therapy, pioneering new markets and changing standards of care with its novel antisense technology. Ionis currently has three marketed medicines and a premier late-stage pipeline highlighted by industry-leading cardiovascular and neurological franchises. Our scientific innovation began and continues with the knowledge that sick people depend on us, which fuels our vision of becoming a leading, fully integrated biotechnology company.

To learn more about Ionis, visit www.ionispharma.com and follow us on Twitter @ionispharma.

Ionis' Forward-looking Statements

This press release includes forward-looking statements regarding Ionis' business and the therapeutic and commercial potential of Ionis' technologies, ION449 and other products in development. 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, including those related to the impact COVID-19 could have on our business, and including but not limited to, those related to our commercial products and the medicines in our pipeline, and particularly those inherent in the process of discovering, developing and commercializing medicines that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such medicines. 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 Dec. 31, 2021, and the most recent Form 10-Q quarterly filing, which are on file with the Securities and Exchange Commission. 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.

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