

Ionis announces third investigational antisense medicine to treat nonalcoholic steatohepatitis (NASH) enters development

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CARLSBAD, Calif., Nov. 23, 2020 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS) announced today that the biopharmaceutical company AstraZeneca has licensed ION455, an investigational antisense medicine being developed as a potential treatment for nonalcoholic steatohepatitis (NASH). ION455 is the second medicine for the treatment of NASH that Ionis has partnered with AstraZeneca. The companies have also partnered on ION839 (AZD2693), which is designed to inhibit the production of patatin-like phospholipase domain-containing 3 (PNPLA3) protein, a major genetic determinant of NASH progression. Separately, Ionis is also developing a wholly owned NASH program. ION224 is designed to reduce the production of DGAT2, or diacylglycerol acyltransferase 2, for treating patients with NASH. ION224 is one of more than 20 medicines in the growing Ionis-owned pipeline that the company is prioritizing and preparing for commercialization.

NASH is the most severe form of nonalcoholic fatty liver disease (NAFLD). It is related to the epidemic of obesity, pre-diabetes and diabetes. Unlike liver disease caused by alcohol consumption, NAFLD is the result of an accumulation of fat in the liver, which can lead to inflammation and cirrhosis, an advanced scarring of the liver that prevents the liver from functioning normally. About 20 percent of NASH patients are reported to develop cirrhosis and 30 to 40 percent of patients with NASH cirrhosis experience liver-related death.ⁱ Currently, a liver transplant is the only treatment for advanced cirrhosis and liver failure. Because of the high prevalence of NASH, it has recently become the third most common indication for liver transplantation in the U.S.

"Today, there are no FDA-approved medicines to specifically treat nonalcoholic steatohepatitis. However, due in large part to the progress made by our cardio-metabolic franchise, three Ionis-discovered novel medicines are now in development. These are encouraging advances that we hope will one day bring therapeutic benefit to patients who have limited treatment options," said Brett P. Monia, Ph.D., Ionis' chief executive officer.

ION455 is the fourth medicine to reach development in partnership with AstraZeneca. Ionis earned \$30 million from AstraZeneca for licensing ION455 and is eligible to earn up to \$300 million in milestone payments plus royalties on net sales. AstraZeneca will have responsibility for further development of ION455, including regulatory filings, and commercialization.

In addition to NASH, Ionis and AstraZeneca are collaborating on potential treatments for kidney disease, cardiovascular disease and cancer.

Ionis' Forward-looking Statement

This press release includes forward-looking statements regarding Ionis' business and the therapeutic and commercial potential of ION455, ION839 (AZD2693), ION224 and Ionis' technologies and 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 December 31, 2019, and the most recent Form 10-Q quarterly filing, 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.

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About Ionis Pharmaceuticals, Inc.

As the leader in RNA-targeted drug discovery and development, Ionis has created an efficient, broadly applicable, drug discovery platform called antisense technology that can treat diseases where no other therapeutic approaches have proven effective. Our drug discovery platform has served as a springboard for actionable promise and realized hope for patients with unmet needs. We created the first and only approved treatment for all patients, children and adults with spinal muscular atrophy, as well as the world's first RNA-targeted therapeutic approved for the treatment of polyneuropathy in adults with hereditary transthyretin amyloidosis. Our sights are set on all the patients we have yet to reach with a pipeline of more than 40 novel medicines designed to potentially treat a broad range of disease, including neurological, cardio-renal, metabolic, infectious, and pulmonary diseases.

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

ⁱ Takahashi, Y. et al. (2015) Current pharmacological therapies for nonalcoholic fatty liver disease/nonalcoholic steatohepatitis. World J Gastroenterol. 21, 3777-3785

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