Ionis enters agreement with Roche for two novel RNA-targeted programs for Alzheimer's disease and Huntington's disease

September 27, 2023

- *Roche gains exclusive worldwide rights to develop, manufacture and commercialize the investigational medicines discovered by Ionis*
- *Ionis to receive a $60 million upfront payment*

CARLSBAD, Calif., Sept. 27, 2023 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today announced that it has entered an agreement with Roche for two undisclosed early-stage programs for RNA-targeting investigational medicines for the treatment of Alzheimer's disease (AD) and Huntington's disease (HD). Roche gains exclusive worldwide rights and will be responsible for clinical development, manufacturing, and commercialization of the medicines if they receive regulatory approval. The companies will leverage Ionis' expertise discovering medicines that target the root cause of central nervous system diseases and Roche's global experience developing and commercializing therapies for nervous system disorders.

"We are excited to expand our partnership with Roche, a global leader in developing and delivering innovative treatments to patients," said Brett P. Monia, Ph.D., Ionis' chief executive officer. "With this new collaboration, we are joining forces to accelerate the discovery and development of novel therapies for people living with Alzheimer's disease and Huntington's disease globally. Collaborating on these two programs enables Ionis to advance our wholly owned programs, including those in neurology, aligned with our strategic priorities."

"Our lasting partnership with Ionis, a leader in RNA-targeted therapeutics, is a great example of two collaborators mutually benefiting from their relationship by complementing and learning from each other," said James Sabry, Ph.D., global head of Roche Pharma partnering. "By expanding our alliance, we bring together the companies' combined knowledge of the science in Alzheimer's disease and Huntington's disease with Roche's proven capabilities in the development and commercialization of innovative treatments in neuroscience."

Under terms of the agreement, Ionis will have responsibility to advance the two programs through pre-clinical studies; Roche will have sole responsibility for clinical development and, if approved, commercialization worldwide. Ionis will receive a $60 million upfront payment from Roche and is eligible to receive development, regulatory and commercial milestone payments, and tiered royalties.

Ionis and Roche have been strong partners for the past 10 years, starting with their collaboration in 2013 for tominersen, an Ionis-discovered investigational medicine for HD. Tominersen, designed to reduce the production of all forms of the huntingtin protein, is currently being evaluated by Roche in a Phase 2 proof of concept study (GENERATION HD2) assessing safety, biomarker and efficacy trends in people with prodromal or early manifest HD. In addition to tominersen, both companies are working together on a pre-clinical stage mutant HTT selective antisense oligonucleotide for HD. The companies entered another collaboration in 2018 to develop IONIS-FB-L_{Rx} targeting Factor B for the treatment of IgA nephropathy (IgAN) and geographic atrophy (GA). IONIS-FB-L_{Rx} is currently in a Phase 2 study for GA, led by Ionis, and a Phase 3 study for IgAN led by Roche.

About Alzheimer's Disease

AD is the most common cause of dementia and, according to the World Health Organization, more than 55 million people have dementia worldwide[1]. During the course of the disease, protein plaques appear in the brain, leading to the death of brain cells. No single factor has been identified as the cause of Alzheimer's disease.

About Huntington's Disease

HD is a rare, genetic, neurodegenerative disease characterized by a triad of cognitive, behavioral, and motor symptoms leading to functional decline, progressive loss of independence, and impacting families across generations. It is caused by the expansion of the cytosine-adenine-guanine (CAG) trinucleotide sequence in the HTT gene. The resulting mutant HTT protein is toxic and gradually destroys neurons. Symptoms usually appear between the ages of 30 and 50 and worsen over a 10 to 25-year period. There is no effective treatment or cure for the disease and currently available medicines only mask the patient's symptoms but do not slow down the underlying loss of neurons.

About Ionis Pharmaceuticals, Inc.

For more than 30 years, Ionis has been a leader in RNA-targeted therapy, pioneering new markets and changing standards of care. Ionis currently has four marketed medicines and a promising late-stage pipeline highlighted by cardiovascular and neurological franchises. Our scientific innovation began and continues with the knowledge that sick people depend on us, which fuels our vision to become the leader in genetic medicine, utilizing a multi-platform approach to discover, develop and deliver life-transforming therapies.

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 tominersen, Ionis' newly initiated programs for Alzheimer's disease and Huntington's disease, IONIS-FB-L_{Rx}, Ionis' technologies 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 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, 2022, 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.

Ionis Pharmaceuticals® is a trademark of Ionis Pharmaceuticals, Inc.

[1] World Health Organization. Dementia. https://www.who.int/news-room/fact-sheets/detail/dementia

View original content to download multimedia:https://www.prnewswire.com/news-releases/ionis-enters-agreement-with-roche-for-two-novel-rna-targeted-programs-for-alzheimers-disease-and-huntingtons-disease-301939627.html

SOURCE Ionis Pharmaceuticals, Inc.

Ionis Investor Contact: D. Wade Walke, Ph.D., info@ionisph.com, 760-603-2331; Ionis Media Contact: David Polk, J.D., ionis_ca@ionisph.com, 760-603-4679