Ionis expands eplontersen agreement with AstraZeneca to include exclusive rights in Latin America

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- *Companies jointly developing and commercializing eplontersen in the U.S.*
- *AstraZeneca adds Latin America as part of its exclusive rights for rest of world*

CARLSBAD, Calif., July 28, 2023 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today announced it has expanded its existing collaboration with AstraZeneca to include exclusive rights for AstraZeneca to commercialize eplontersen in Latin America. Ionis previously granted AstraZeneca exclusive rights to commercialize eplontersen in all other countries outside the U.S. Ionis and AstraZeneca will continue to jointly develop and commercialize eplontersen in the U.S. The companies are successfully advancing eplontersen by combining Ionis' industry-leading expertise in RNA-targeted therapeutics and deep knowledge of transthyretin amyloidosis (ATTR) with AstraZeneca's global cardiovascular commercial capabilities.

Eplontersen is an investigational antisense medicine discovered by Ionis that reduces the production of transthyretin protein (TTR) to treat ATTR, a systemic, progressive, and fatal disease.

"The positive clinical results from our Phase 3 NEURO-TTRansform study, combined with eplontersen's self-administration profile, reinforce eplontersen's potential to be an important and differentiated new treatment option for patients with ATTR," said Brett P. Monia Ph.D., chief executive officer of Ionis. "With FDA review of eplontersen for ATTR polyneuropathy already underway and plans to file for regulatory approval in the EU and other countries later this year, today's agreement underscores our shared commitment to ensuring that this much needed treatment is made available to patients around the world."

AstraZeneca paid Ionis $20 million to license eplontersen in Latin America.

Under the terms of the collaboration agreement, Ionis is eligible to receive up to $3.6 billion in milestone and other payments. The collaboration includes territory-specific cost-sharing provisions. Ionis is also eligible to earn royalties in the range of low double-digit to mid-20s percentage depending on region.

Ionis and AstraZeneca are seeking regulatory approval for eplontersen for the treatment of hereditary transthyretin-mediated amyloid polyneuropathy (ATTRv-PN) in the U.S. and plan to seek regulatory approval in the EU and other parts of the world. The U.S. Food and Drug Administration accepted the New Drug Application for eplontersen for the treatment of ATTRv-PN with a PDUFA action date of Dec. 22, 2023. Eplontersen was granted Orphan Drug Designation in the U.S.

Eplontersen is currently being evaluated in the Phase 3 CARDIO-TTRansform study (NCT04136171) for transthyretin-mediated amyloid cardiomyopathy (ATTR-CM), a systemic, progressive and fatal condition that typically leads to progressive heart failure and often death within three to five years from disease onset.

About Eplontersen

Eplontersen is an investigational **LI**gand-**C**onjugated **A**ntisense (LICA) medicine designed to inhibit the production of TTR protein. Eplontersen is being developed as a monthly self-administered subcutaneous injection to treat all types of ATTR. ATTR amyloidosis is a systemic, progressive and fatal disease in which patients experience multiple overlapping clinical manifestations caused by the inappropriate formation and aggregation of TTR amyloid deposits in various tissues and organs, including peripheral nerves, heart, intestinal tract, eyes, kidneys, central nervous system, thyroid and bone marrow. The progressive accumulation of TTR amyloid deposits in these tissues and organs leads to organ failure and eventually death.

About Transthyretin Amyloidosis (ATTR)

Transthyretin amyloidosis (ATTR) is a systemic, progressive and fatal disease in which patients experience multiple overlapping clinical manifestations caused by the inappropriate formation and aggregation of TTR amyloid deposits in various tissues and organs, including peripheral nerves, heart, intestinal tract, eyes, kidneys, central nervous system, thyroid and bone marrow. The progressive accumulation of TTR amyloid deposits in these tissues and organs leads to organ failure and eventually death.

Hereditary transthyretin-mediated amyloid polyneuropathy (ATTRv-PN) is caused by the accumulation of misfolded mutated TTR protein in the peripheral nerves. Patients with ATTRv-PN experience ongoing debilitating nerve damage throughout their body resulting in the progressive loss of motor functions, such as walking. These patients also accumulate TTR in other major organs, which progressively compromises their function. The damage from misfolded TTR protein accumulation leads to disability within five years of diagnosis and is generally fatal within a decade.

Transthyretin-mediated amyloid cardiomyopathy (ATTR-CM) is an underdiagnosed and fatal disease. It is caused by the accumulation of misfolded TTR protein in the cardiac muscle. Patients experience ongoing debilitating heart damage resulting in progressive heart failure, which results in death within three to five years from disease onset. ATTR cardiomyopathy includes both the genetic and wild-type form of the disease.

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 eplontersen, 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" all refer to Ionis Pharmaceuticals and its subsidiaries.

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