Ionis announces eplontersen receives orphan drug designation from U.S. FDA

January 24, 2022

CARLSBAD, Calif., Jan. 24, 2022 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS), the leader in antisense therapeutics, announced today that the U.S. Food and Drug Administration (FDA) has granted orphan drug designation to eplontersen, an investigational antisense medicine for the treatment of people living with transthyretin-mediated amyloidosis, a systemic, progressive and fatal condition. Orphan drug designation is granted by the FDA to drugs and biologics intended for treatment, prevention or diagnosis of a rare disease or condition that affects fewer than 200,000 people in the U.S. at the time of designation.

Eplontersen is a **LI**gand-**C**onjugated **A**ntisense (LICA) investigational medicine currently in Phase 3 clinical trials for amyloid transthyretin cardiomyopathy (ATTR-CM) and amyloid transthyretin polyneuropathy (ATTR-PN). It is designed to reduce the production of transthyretin (TTR protein) to treat both hereditary and non-hereditary forms of TTR amyloidosis (ATTR). In December 2021, Ionis announced a strategic collaboration with AstraZeneca to develop and commercialize eplontersen.

ATTR-CM is a systemic, progressive and fatal condition that leads to progressive heart failure and death within four years from diagnosis. It remains underdiagnosed and its prevalence is thought to be underestimated due to a lack of disease awareness and the heterogeneity of symptoms. Hereditary ATTR-PN is a debilitating disease that leads to peripheral nerve damage with motor disability within five years of diagnosis and, without treatment, is generally fatal within a decade.

Under the FDA's Orphan Drug Act, orphan drug status provides incentives, including tax credits, grants and waiver of certain administrative fees for clinical trials, and seven years of market exclusivity following drug approval.

"Receiving FDA orphan drug status for eplontersen underscores the significant unmet need for novel treatment options for people living with transthyretin-mediated amyloidosis. We look forward to working closely with regulators, clinical investigators, patients and their families to advance this important medicine and make it available to those who may benefit from it," said Richard S. Geary, Ph.D., executive vice president and chief development officer at Ionis.

About eplontersen

Eplontersen (formerly IONIS-TTR-L_{Rx}) is an investigational antisense medicine that uses Ionis' **LI**gand-**C**onjugated **A**ntisense (LICA) technology and is designed to reduce the production of transthyretin, or TTR protein, to treat all types of TTR amyloidosis (ATTR), a systemic, progressive, and fatal disease. Ionis and AstraZeneca are currently evaluating eplontersen in the CARDIO-TTRansform Phase 3 study for the treatment of patients with hereditary and wild-type cardiomyopathy (ATTR-CM) and the NEURO-TTRansform Phase 3 study for the treatment of patients with hereditary transthyretin-mediated amyloid polyneuropathy (hATTR-PN).

About TTR Amyloidosis (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.

Polyneuropathy due to hATTR is caused by the accumulation of misfolded mutated TTR protein in the peripheral nerves. Patients with polyneuropathy due to hATTR 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 compromise their function and, without treatment is generally fatal within a decade.

ATTR cardiomyopathy 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 four years from diagnosis. 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 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 neurological and cardiometabolic franchises. Our scientific innovation began and continues with the knowledge that sick people depend on us, which fuels our vision of becoming one of the most successful biotechnology companies.

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

Forward-looking Statements

This press release includes forward-looking statements regarding Ionis' business and the therapeutic and commercial potential of Ionis' technologies, eplontersen 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, 2020, 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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