Eplontersen continued to show improvement in ATTRv-PN through 85 weeks

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- *Topline Phase 3 NEURO-TTRansform results show eplontersen continued to halt neuropathy disease progression and improve quality of life through 85 weeks*
- *Data further strengthen eplontersen's differentiated profile, positioning it to be an important potential treatment for patients with ATTRv-PN*

CARLSBAD, Calif., July 10, 2023 /PRNewswire/ -- Ionis Pharmaceuticals (Nasdaq: IONS) today announced positive topline, 85-week data from the Phase 3 NEURO-TTRansform study in patients with hereditary transthyretin-mediated amyloid polyneuropathy (ATTRv-PN). Ionis and AstraZeneca's eplontersen continued to show sustained improvements in measures of neuropathy disease and a favorable safety and tolerability profile.

An overview of key results from the 85-week topline analysis is available here. At 85 weeks, eplontersen continued to show a sustained reduction in serum TTR concentration compared to baseline and continued to halt disease progression as measured by the modified Neuropathy Impairment Score +7 (mNIS+7). Eplontersen also showed continued improvement on the Norfolk Quality of Life Questionnaire-Diabetic Neuropathy (Norfolk QoL-DN) compared to baseline. Results from the NEURO-TTRansform primary analysis at 66 weeks were presented earlier this year.

"These positive findings further strengthen eplontersen's efficacy and safety profile, underscoring its potential to be an important, differentiated advancement for patients with this progressive, debilitating and fatal disease," said Eugene Schneider, M.D., Ionis' executive vice president and chief clinical development officer. "A substantial number of eplontersen-treated patients showed improvement in neuropathy impairment and quality of life through 19 months of treatment. ATTRv-PN continues to be an underserved patient population and we look forward to working with regulatory authorities to bring this important new, self-administered treatment to patients."

Results from the 85-week exploratory analysis of NEURO-TTRansform will be submitted for presentation at an upcoming medical meeting. As part of a global development and commercialization agreement, Ionis and AstraZeneca are seeking regulatory approval for eplontersen for the treatment of ATTRv-PN in the U.S. and plan to seek regulatory approval in Europe 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 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 Hereditary Transthyretin-Mediated Amyloid Polyneuropathy (ATTRv-PN)

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.

About the NEURO-TTRansform Study

NEURO-TTRansform is a global, open-label, randomized trial evaluating the efficacy and safety of eplontersen in patients with ATTRv-PN at week 35, week 66 and week 85. The final analysis comparing eplontersen to an external placebo group was completed at week 66. All patients were then followed on treatment until week 85 and evaluated four weeks after the last dose in an end-of-trial assessment. Following treatment and the end-of-trial assessments, patients were eligible to enter an open-label extension study to continue receiving eplontersen once every four weeks or enter a 20-week post-treatment evaluation period. For more information on the NEURO-TTRansform study, please visit: https://clinicaltrials.gov/ct2/show/NCT04136184

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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