New data from the Phase 3 NEURO-TTRansform study evaluating WAINUA™ (eplontersen) to be presented at the 2024 International Symposium on Amyloidosis (ISA)

May 23, 2024

– Results across NEURO-TTRansform subgroups show consistent benefit in neuropathy impairment and improved quality of life, regardless of patient segmentation –

CARLSBAD, Calif., May 23, 2024 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) announced today that it will present new subgroup analyses from Ionis and AstraZeneca's Phase 3 NEURO-TTRansform study of WAINUA™ (eplontersen) at the 2024 International Symposium on Amyloidosis (ISA) in Rochester, Minnesota, May 26-30. WAINUA was approved by the U.S. Food and Drug Administration (FDA) in December 2023 for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults, commonly referred to as hATTR-PN or ATTRv-PN.

Notable presentations include:

- **Neuropathy Impairment and Nutritional Status with Eplontersen in Patients with Hereditary Transthyretin-Mediated Amyloidosis**
  - Abstract ID 174: May 29, 2024, 10:00-10:30 am ET (poster presentation 1) and 2:45-3:45 pm ET (poster presentation 2)
  - Presenting Author: Jonas Wixner
- **Eplontersen for Hereditary Transthyretin Amyloidosis with Polyneuropathy: An Exploratory Analysis in Patients with the V30M *TTR* Variant and Early-Onset or Late-Onset Disease**
  - Abstract ID 230: May 29, 2024, 10:00-10:30 am ET (poster presentation 1) and 2:45-3:45 pm ET (poster presentation 2)
  - Presenting Author: Julian D. Gillmore
- **Eplontersen for Hereditary Transthyretin Amyloidosis with Polyneuropathy: An Exploratory Analysis of Treatment Effect in Male and Female Patients**
  - Abstract ID 202: May 29, 2024, 10:00-10:30 am ET (poster presentation 1) and 2:45-3:45 pm ET (poster presentation 2)
  - Presenting Author: Márcia Waddington Cruz

As part of a global development and commercialization agreement, AstraZeneca and Ionis are commercializing WAINUA for the treatment of ATTRv-PN in the U.S. and are seeking regulatory approval in Europe and other parts of the world.

Eplontersen is currently being evaluated in the Phase 3 CARDIO-TTRansform study for adults with 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. The CARDIO-TTRansform Phase 3 study is fully enrolled with more than 1,400 patients – making it the largest study in this patient population to date.

About WAINUA™ (eplontersen)
WAINUA™ (eplontersen) is a**L**igand-**C**onjugated **A**ntisense (LICA) medicine designed to inhibit the production of transthyretin, or TTR protein. WAINUA has been approved in the U.S. for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults (also referred to as ATTRv-PN). Please see full Prescribing Information.

INDICATION for WAINUA™ (eplontersen)
WAINUA injection for subcutaneous use 45 mg is indicated for treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

IMPORTANT SAFETY INFORMATION for WAINUA™ (eplontersen)

WARNINGS AND PRECAUTIONS
Reduced Serum Vitamin A Levels and Recommended Supplementation WAINUA leads to a decrease in serum vitamin A levels. Supplement with recommended daily allowance of vitamin A. Refer patient to an ophthalmologist if ocular symptoms suggestive of vitamin A deficiency occur.

ADVERSE REACTIONS

Most common adverse reactions (≥9% in WAINUA-treated patients) were vitamin A decreased (15%) and vomiting (9%).

Please see link to U.S. Full Prescribing Information for WAINUA.

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.

About Hereditary Transthyretin-Mediated Amyloid Polyneuropathy (ATTRv-PN)

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 Ionis Pharmaceuticals, Inc.

For three decades, Ionis has invented medicines that bring better futures to people with serious diseases. Ionis currently has five marketed medicines and a leading pipeline in neurology, cardiology, and other areas of high patient need. As the pioneer in RNA-targeted medicines, Ionis continues to drive innovation in RNA therapies in addition to advancing new approaches in gene editing. A deep understanding of disease biology and industry-leading technology propels our work, coupled with a passion and urgency to deliver life-changing advances for patients. To learn more about Ionis, visit Ionispharma.com and follow us on X (Twitter) and LinkedIn.

Forward-looking Statements

This press release includes forward-looking statements regarding eplontersen, Ionis' business, and the therapeutic and commercial potential of Ionis' commercial medicines, additional medicines in development and technologies. 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 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. Except as required by law, we undertake no obligation to update any forward-looking statements for any reason. 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, 2023, and most recent Form 10-Q, which are on file with the SEC. Copies of these and other documents are available at www.ionispharma.com.

Ionis Pharmaceuticals Investor Contact: D. Wade Walke, Ph.D. - info@ionisph.com - 760-603-2331; **Ionis Pharmaceuticals Media Contact:** Daria Binder - CorporateCommunications@ionisph.com - 760-603-4679

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