



WAINUA™ (eplontersen) granted regulatory approval in the U.S. for the treatment of adults with polyneuropathy of hereditary transthyretin-mediated amyloidosis

December 21, 2023

- U.S. FDA approval based on Phase 3 NEURO-TTRansform results showing WAINUA demonstrated consistent and sustained benefit halting neuropathy disease progression and improving neuropathy impairment and quality of life
- Additional regulatory reviews for WAINUA underway in rest of world
- WAINUA will be available in the U.S. in January 2024

CARLSBAD, Calif., Dec. 21, 2023 /PRNewswire/ -- [Ionis Pharmaceuticals, Inc.](#) (Nasdaq: IONS) announced today that the U.S. Food and Drug Administration (FDA) has approved Ionis and AstraZeneca's WAINUA™ (eplontersen) for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults, commonly referred to as hATTR-PN or ATTRv-PN. WAINUA is the only approved medicine for the treatment of ATTRv-PN that can be self-administered via an auto-injector.



The approval was based on the [positive 35-week interim analysis from the Phase 3 NEURO-TTRansform study](#) which showed patients treated with WAINUA demonstrated consistent and sustained benefit on the co-primary endpoints of serum transthyretin (TTR) concentration and neuropathy impairment measured by modified Neuropathy Impairment Score +7 (mNIS+7), and key secondary endpoint of quality of life (QoL) on the Norfolk Quality of Life Questionnaire-Diabetic Neuropathy (Norfolk QoL-DN). Positive results from the Phase 3 NEURO-TTRansform study were published in [The Journal of the American Medical Association \(JAMA\)](#) further demonstrating the benefit of WAINUA across the spectrum of ATTRv-PN at 35, 66 and 85-weeks.

"Many people living with hereditary transthyretin-mediated amyloid polyneuropathy are unable to fully enjoy their lives because of the relentless, progressive and debilitating effects of the disease," said Michael J. Polydefkis, M.D., professor of neurology at Johns Hopkins University School of Medicine and an investigator in the NEURO-TTRansform study. "Approval of WAINUA represents a meaningful advancement in treatment, one that gives those who are living with transthyretin-mediated amyloid polyneuropathy help managing the disease."

ATTRv-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. WAINUA is a ligand-conjugated antisense oligonucleotide (LICA) medicine designed to reduce the production of TTR protein at its source.

"The FDA approval of WAINUA marks an important milestone for people living with hereditary transthyretin-mediated amyloid polyneuropathy, who will now have an effective, well-tolerated treatment that can be self-administered via auto-injector to combat this devastating disease," said Brett P. Monia, Ph.D., chief executive officer at Ionis. "It is also a pivotal moment for Ionis as WAINUA will be the first in a steady cadence of potential commercial launches for the company. We are proud to have discovered and, together with AstraZeneca, developed WAINUA, and are grateful to the patients, caregivers and investigators who participated in our clinical studies, as well as for the dedication of our scientists and researchers."

"People with hereditary transthyretin-mediated amyloid polyneuropathy, and other forms of amyloidosis, are often misdiagnosed since symptoms can mirror other conditions," said Isabelle Lousada, President and CEO, Amyloidosis Research Consortium "The path to getting an accurate diagnosis can often be a long, arduous journey and it is critical that a timely and accurate diagnosis is made not only for the individual experiencing symptoms but for their families and loved ones. It is exciting to see new innovations coming through and increased efforts to raise awareness in an area that has often been overlooked or neglected."

WAINUA will be available in the U.S. in January 2024.

"There is an urgent medical need for new therapies for people living with hereditary transthyretin-mediated amyloid polyneuropathy," said Ruud Dobber, executive vice president, BioPharmaceuticals Business Unit, AstraZeneca. "The U.S. approval of WAINUA offers a new treatment option that provides consistent and sustained reduction in serum TTR concentration compared to baseline while halting disease progression and improving quality of life for people living with this debilitating condition."

As part of a [global development and commercialization agreement](#), AstraZeneca and Ionis will commercialize WAINUA for the treatment of ATTRv-PN in the U.S. and are seeking regulatory approval in Europe and other parts of the world. This agreement was recently expanded to include exclusive rights for AstraZeneca to commercialize WAINUA in Latin America in addition to all other countries outside the U.S. WAINUA was [granted Orphan Drug Designation](#) in the U.S. and in the EU for the treatment of transthyretin-mediated amyloidosis (ATTR).

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. 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 ligand-conjugated antisense (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 ($\geq 9\%$ in WAINUA-treated patients) were vitamin A decreased (15%) and vomiting (9%).

Please see link to [U.S. Full Prescribing Information](#) for WAINUA.

About 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 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 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 WAINUA, 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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