Eplontersen granted U.S. FDA Fast Track designation for patients with transthyretin-mediated amyloid cardiomyopathy

February 8, 2024

CARLSBAD, Calif., Feb. 8, 2024 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) announced today that the U.S. Food and Drug Administration (FDA) has granted Fast Track designation to Ionis and AstraZeneca's eplontersen, an investigational therapy for the treatment of transthyretin-mediated amyloid cardiomyopathy (ATTR-CM) in adults. The FDA grants development programs Fast Track designation to facilitate the development and expedite the review of drugs that demonstrate the potential to treat serious conditions and fill an unmet medical need.

"Receiving Fast Track designation from the FDA reinforces our belief that eplontersen has the potential to be a transformational treatment for patients with ATTR-CM, which remains a progressive and fatal condition for hundreds of thousands of people worldwide despite available treatment options," said Eugene Schneider, M.D., executive vice president and chief clinical development officer, Ionis. "CARDIO-TTRansform is the largest, most comprehensive study ever conducted in ATTR-CM patients, with results expected as early as next year."

Sarah Walters, vice president, U.S. cardiovascular, renal and metabolic diseases, AstraZeneca said: "We are committed to accelerating innovation and addressing the spectrum of unmet patient needs in amyloidosis. Together with our partner Ionis, AstraZeneca is building on our heritage in cardiovascular disease and RNA-targeted therapeutics to bring a potential best-in-class treatment for people living with ATTR-CM."

In December 2023, eplontersen was approved in the U.S. for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults, commonly referred to as hATTR-PN or ATTRv-PN, under the brand name WAINUA™ (eplontersen). 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. WAINUA was granted Orphan Drug Designation in the U.S. and in the EU for the treatment of transthyretin-mediated amyloidosis (ATTR).

The global CARDIO-TTRansform Phase 3 study of eplontersen in adults with ATTR-CM is fully enrolled with more than 1,400 patients – making it the largest study in this patient population to date. The company plans to share data from the CARDIO-TTRansform study as early as 2025. More information on the CARDIO-TTRansform study (NCT04136171) is available at www.clinicaltrials.gov.

About Transthyretin-Mediated Amyloid Cardiomyopathy (ATTR-CM)

Transthyretin-mediated amyloid cardiomyopathy (ATTR-CM) is an underdiagnosed and potentially 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-CM includes both the genetic and wild-type form of the disease. Worldwide, there are an estimated 300,000 – 500,000 patients with ATTR-CM.[1,2,3]

About Eplontersen

Eplontersen is a **LI**gand-**C**onjugated **A**ntisense (LICA) medicine designed to inhibit the production of transthyretin, or TTR protein. The investigational medicine is currently being evaluated in the Phase 3 CARDIO-TTRansform study for hereditary or wild-type transthyretin-mediated amyloid cardiomyopathy (ATTR-CM), a 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.

Eplontersen was recently approved in the U.S. for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults, commonly referred to as hATTR-PN or ATTRv-PN under the brand name WAINUA™ (eplontersen). Please see fulPrescribing 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 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.

Ionis' 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. 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 most recent Form 10-Q, which are on file with the SEC. Copies of these and other documents are available at www.ionispharma.com.

[1] Mohamed-Salem L, et al. Prevalence of wild type ATTR assessed as myocardial uptake in bone scan in the elderly population. Int J Cardiol. 2018 Nov 1;270:192-196. doi: 10.1016/j.ijcard.2018.06.006.

[2] Cuscaden C, et al. Estimation of prevalence of transthyretin (ATTR) cardiac amyloidosis in an Australian subpopulation using bone scans with echocardiography and clinical correlation. J Nucl Cardiol. 2020 May 8. doi: 10.1007/s12350-020-02152-x.

[3] Columbia University Irving Medical Center [Internet]. Drug Reduces Death from Underdiagnosed Form of Heart Failure [last accessed 5 February 2024]. Available from: https://www.cuimc.columbia.edu/news/drug-reduces-deaths-underdiagnosed-form-heart-failure.

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