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AstraZeneca PLC
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# *Wainzua (eplontersen) recommended for approval in the EU by CHMP for the treatment of adult patients with polyneuropathy associated with hereditary transthyretin-mediated amyloidosis*

***Recommendation based on NEURO-TTRansform Phase III results showing Wainzua demonstrated consistent and sustained benefit improving neuropathy impairment and quality of life versus placebo***

AstraZeneca and Ionis' *Wainzua* (eplontersen) has been recommended for approval by the Committee for Medicinal Products for Human Use (CHMP) in the European Union (EU) for the treatment of hereditary transthyretin-mediated amyloidosis in adult patients with stage 1 or stage 2 polyneuropathy, commonly referred to as hATTR-PN or ATTRv-PN.[1] If approved by the European Commission, *Wainzua* will be the only approved medicine in the EU for the treatment of ATTRv-PN that can be self-administered monthly via an auto-injector.[2-7]

The CHMP based its opinion on the positive NEURO-TTRansform Phase III trial which showed that through 66 weeks, patients treated with *Wainzua* 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) versus external placebo.[2,8] *Wainzua* continued to demonstrate a favourable safety and tolerability profile throughout the NEURO-TTRansform trial.[2,8]

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.[9,10]

Dr Laura Obici, Head of Rare Diseases Unit, Consultant at the Amyloidosis Research and Treatment Centre Istituto Di Ricovero e Cura a Carattere Scientifico Fondazione Policlinico San Matteo, Pavia, Italy, said: "This debilitating disease is ultimately fatal if left untreated and can have a significant impact on many aspects of patients' and caregivers' day-to-day lives. Having additional amyloidosis treatment options designed to reduce the production of TTR protein at its source would potentially give patients more time and ability to do what matters most to them and offer the hope of living longer with a higher quality of life."

Ruud Dobber, Executive Vice-President, BioPharmaceuticals Business Unit, AstraZeneca, said: "Due to the progressive nature of polyneuropathy of hereditary transthyretin-mediated amyloidosis, it is critical to have timely diagnosis and new therapies to help people have greater control over this potentially fatal disease. Today's recommendation brings *Wainzua* one step closer for patients in Europe, and if approved, will offer a new treatment option that can provide consistent TTR suppression and results in improved quality of life."

*Wainzua* is a once-monthly silencer that provides upstream suppression of TTR production.[2,3,11] It is an RNA-targeted medicine designed to reduce production of TTR protein at its source in the liver to potentially treat all types of transthyretin-mediated amyloidosis (ATTR).[2,3,11]

*Wainzua* was approved under the brand name *Wainua* for the treatment of ATTRv-PN in the US in December 2023 and is now gaining approvals in additional countries worldwide.[11,12] As part of a global development and commercialisation agreement, AstraZeneca and Ionis are commercialising *Wainua* for the treatment of ATTRv-PN in the US.[11,12] The companies are seeking regulatory approval in the EU and other parts of the world, where AstraZeneca has exclusive rest of world commercialisation and development rights. Eplontersen was granted Orphan Drug Designation in the US and in the EU for the treatment of ATTR.[11,12]

Eplontersen is currently being evaluated in the CARDIO-TTRansform Phase III trial for treatment of transthyretin-mediated amyloid cardiomyopathy (ATTR-CM), the largest of all ATTR-CM trials to date including over 1,400 participants.[11-14]

## Notes

### TTR Amyloidosis

ATTR is caused by the accumulation of liver-derived misfolded TTR protein in tissues, such as the heart and the peripheral nerves, causing organ damage and failure.[2,15] ATTR then causes complications, leading to cardiovascular, neurological and renal diseases such as heart failure (HF) and chronic kidney disease.[15,16] There are both hereditary (ATTRv) and non-hereditary (wild-type) forms of ATTR. [15] ATTR is a rapidly progressive and fatal disease that requires timely recognition of symptoms.[15,17] ATTR has several phenotypes including ATTR-CM, which predominantly impacts the heart, potentially leading to HF, ATTRv-PN, which predominantly affects the peripheral nervous system, and mixed phenotype, where patients experience symptoms of both.[15,18] Worldwide, there are an estimated 300,000 - 500,000 patients with ATTR-CM and about 10,000 - 40,000 patients with ATTRv-PN.[11,18]

### NEURO-TTRansform

NEURO-TTRansform is a global, open-label, randomised trial evaluating the efficacy and safety of eplontersen in patients with ATTRv-PN.[2,19] The trial enrolled adult patients with ATTRv-PN Stage 1 or Stage 2 compared to the external placebo.[2,19] The comparison of efficacy and safety for eplontersen versus external placebo was based on data up to week 66.[2,19] All patients were then followed on treatment until week 85 and evaluated four weeks after the

data up to week 66.[2,19] All patients were then followed on treatment until week 85 and evaluated four weeks after the last dose in an end-of-trial assessment.[2,19] Following treatment and the end-of-trial assessments, patients were eligible to enter an open-label extension study, which is still ongoing.[2] Full results from the NEURO-TTRansform trial were published in *The Journal of the American Medical Association (JAMA)* further demonstrating the benefit of *Wainzua* across the spectrum of ATTRv-PN at 35, 66 and 85 weeks of treatment.[2,19]

***Wainzua***

*Wainzua* is a once-monthly silencer that provides upstream suppression of TTR production.[2,3,11] It is an RNA-targeted medicine designed to reduce production of TTR protein at its source in the liver to potentially treat all types of ATTR.[2,3,11]

**AstraZeneca in CVRM**

Cardiovascular, Renal and Metabolism (CVRM), part of BioPharmaceuticals, forms one of AstraZeneca's main disease areas and is a key growth driver for the Company. By following the science to understand more clearly the underlying links between the heart, kidneys, liver and pancreas, AstraZeneca is investing in a portfolio of medicines for organ protection by slowing or stopping disease progression, and ultimately paving the way towards regenerative therapies. The Company's ambition is to improve and save the lives of millions of people, by better understanding the interconnections between CVRM diseases and targeting the mechanisms that drive them, so we can detect, diagnose and treat people earlier and more effectively.

**AstraZeneca**

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## Contacts

For details on how to contact the Investor Relations Team, please click here. For Media contacts, click here.

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