News Release

AstraZeneca demonstrates commitment to patients living with amyloidosis at the 2024 International Symposium on Amyloidosis (ISA)

Additional clinical and real-world data from the industry's largest amyloidosis pipeline will advance understanding of underlying mechanisms of disease and unmet needs

WILMINGTON, Del., May 23, 2024 – AstraZeneca and Alexion, AstraZeneca Rare Disease, will showcase 14 studies, including real-world evidence (RWE), from their portfolio and pipeline of investigational amyloidosis therapies at the International Symposium on Amyloidosis (ISA), in Rochester, MN from May 26–30, 2024.

Presentations will include a new subgroup analyses of the Phase 3 NEURO-TTRansform study of WAINUA™ (eplontersen), which was approved by the US 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.[1] Additionally, clinical data will be presented on ALXN2220 and anselamimab, which are being evaluated in Phase III clinical trials for ATTR and light chain (AL) amyloidosis, respectively.

Sarah Walters, Vice President, US Cardiovascular, Renal & Metabolic Diseases, AstraZeneca, said: "AstraZeneca is dedicated to advancing the science and improving the lives of patients that are impacted by this devastating disease. Our data at the 2024 International Symposium on Amyloidosis demonstrate the leadership commitment AstraZeneca, Alexion and our partners Ionis and Neurimmune have to develop best in class treatment options to serve a broad range of amyloidosis patients."

Christophe Hotermans, Senior Vice President, Head of Global Medical Affairs, Alexion, said: "With the largest and fastest-growing pipeline of investigational amyloidosis therapies, we are working to advance multiple modalities with the potential to halt, reduce or reverse organ damage. Key presentations at the ISA Annual Meeting include live-cell imaging and Phase I clinical data evaluating the ability of ALXN2220 to remove amyloid from cardiac tissue, to support its further study as a potential treatment for advanced ATTR cardiomyopathy. Additionally, findings on epidemiology and patient renal outcomes will reinforce the urgency for differentiated amyloidosis diagnosis and additional treatment options in AL amyloidosis."

Robust evidence program increases understanding of amyloidosis patient characteristics and treatment effectiveness.

In addition to sub-analyses of the NEURO-TTRansform data, AstraZeneca and Ionis will present US patient characteristics data, preliminary data from the OverTTuRe study measuring prevalence and characteristics of phenotypes in patients with ATTR amyloidosis in the United States and Japan will be presented; as well as the MaesTTRo study design, part

of a global, multi-study, real-world evidence program designed to fill the evidence gaps of the effectiveness of treatments for ATTR.

WAINUA is currently being evaluated in the Phase 3 CARDIO-TTRansform study for adults with cardiomyopathy of transthyretin-mediated amyloidosis (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.[2-5] 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.[6]

As part of a global development and commercialization agreement, AstraZeneca and Ionis are commercializing WAINUA for the treatment of hATTR-PN in the US and are seeking regulatory approval in Europe and other parts of the world.[6]

Novel investigational amyloid depleter assets demonstrate potential to improve outcomes for amyloidosis patients

High-resolution live-cell imaging will offer new insight into the underlying cellular mechanism of antibody-mediated amyloid removal with ALXN2220. Results will show the addition of ALXN2220 to ATTR patient-derived cardiac tissue triggered phagocytosis, including recruitment of macrophages to amyloid deposits, detachment, internalization and degradation of ATTR amyloid.

An encore poster presentation will report results from the first-in-human study of ALXN2220. Initial treatment with ALXN2220 was well tolerated with a transient increase in C-reactive proteins, suggesting initial targeted immune activation and recruitment of phagocytic immune cells. Additionally, an encore poster presentation will describe the pharmacokinetic and pharmacodynamic (PK/PD) model used for the selection of the dose range, dose escalation, dosing interval and study duration.

Further, a poster will outline the baseline demographics and characteristics of the 406 participants of the Alexion CARES clinical program evaluating anselamimab in patients with Mayo Stage IIIa and IIIb AL amyloidosis, which includes the largest prospective AL amyloidosis study to date in advanced stage AL amyloidosis.

Advancing understanding of the amyloidosis landscape

A retrospective chart analysis from the US EMR TriNetX database will report outcomes in AL amyloidosis patients with renal involvement receiving bortezomib or daratumumab. Only half of patients were renal-responders and few achieved renal complete response (renCR, proteinuria ≤200 mg/day), underscoring the unmet medical need for this patient subset.

Retrospective analyses will also be presented across three posters on the incidence and prevalence of AL and ATTR amyloidosis, reinforcing the importance of timely diagnosis of amyloidosis and continued monitoring.

A comprehensive list of AstraZeneca key abstracts to be presented at the 2024 International Symposium on Amyloidosis includes[7]:

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Lead author	Abstract title	Presentation details Poster presentation session 1: 10:00-10:30 Poster presentation session 2: 14:45-15:45
Eplontersen		
Gillmore JD, Davis M, Hahn K, Smith G, Shivappa N, Papas M, Folkvaljon F, Pao C, Sundin AK, L Wittbrodt E, Grogan M	Prospective, Real-World Data on the Characteristics, Treatment Patterns, and Outcomes of Patients With Transthyretin Amyloidosis: Design of the MaesTTRo Study	Date: Wednesday, May 29 Abstract ID: 204
Waddington Cruz M, Berk J, Parman Y, Gertz M, Khella S, Weiler M, Kwoh J, Chen J, Reicher B, Nåtman J, Dasgupta N	Eplontersen for Hereditary Transthyretin Amyloidosis With Polyneuropathy: An Exploratory Analysis of Treatment Effect in Male and Female Patients	Date: Wednesday, May 29 Abstract ID: 202
Gillmore JD, Adams D, Weiler M, Masri A, Obici L, Kwoh J, Reicher B, Chen J, Waddington Cruz M, Natman J, Gertz M	Eplontersen for Hereditary Transthyretin Amyloidosis With Polyneuropathy: An Exploratory Analysis in Patients With the V30M TTR variant and Early-onset or Late-onset Disease	Date: Wednesday, May 29 Abstract ID: 230
Wixner J, Conceição I, Berk J, Adams D, Polydefkis M, Attarian S, Gillmore J, Dyck J, Coelho T, Chen J, Hardy E, Kwoh J, Nåtman J, Waddington Cruz M	Neuropathy Impairment and Nutritional Status With Eplontersen in Patients With Hereditary Transthyretin-Mediated Amyloidosis	Date: Wednesday, May 29 Abstract ID: 174
Alexander K, Alvarez C, Kumar N, Pao C, Wittbrodt E, Kohsaka S	Prevalence and Descriptive Characteristics of Clinical Phenotypes in Patients With ATTR amyloidosis in the United States and Japan: Preliminary Results from the OverTTuRe Study	Date: Monday, May 27 Abstract ID: 198
Bazell C, Alston M, Kumar N, Huang J, Venditto J, Grillis D, Eisenberg S, Nativi-Nicolau J	Descriptive Characteristics of Patients Diagnosed With Transthyretin Amyloidosis in the Commercial and Medicare Populations	Date: Wednesday, May 29 Abstract ID: 518
ALXN 2220		
Michalon A, Huy, Mercuri M, Kahr P, Hock C,	ALXN2220: High-resolution Live-cell Imaging of Antibody-	Date: Tuesday, May 28

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Grimm J	mediated Cardiac ATTR Amyloid Depletion	Abstract ID: 226
Michalon A, Renaud L, Machacek M, Cortijo C, Udaata C, Mercuri M, Buller F, Hock C, Nitsch R, Kahr P, Grimm J	Prediction of Cardiac ATTR Depletion by NI006 Using Mechanistic PK/PD Modeling	Date: Wednesday, May 29 Abstract ID: 291
Aus dem Siepen F, Van der Meer P, Damy T, Garcia-Pavia P, Donal E, Lairez O, Blank A, Kristen A, Quarta CC, Buchele G, Mercuri M, Hock C, Michalon A, Kahr P, Rey S, Tichy M	ALXN2220: Targeted Immune Activation in Patients Undergoing Antibody-mediated Cardiac ATTR Amyloid Depletion	Date: Wednesday, May 29 Abstract ID: 227
Amyloidosis Incidence and Analyses		
Laires PA, Evans J, Thompson J, Manwani R, Mudumby P, Field M, Fang S	Prevalence, Incidence, and Characterization of Light Chain Amyloidosis in the USA: A Real-World Analysis Utilizing Electronic Health Records (EHR)	Date: Monday, May 27 Abstract ID: 65
Manwani R, Yang F, Zhang Y, Laires PA	Outcomes in Patients With AL Amyloidosis With Renal Involvement: Findings from the TriNetX Database	Date: Monday, May 27 Abstract ID: 113
Laires PA, Li SXL, Uday A, Kumar P, Silva AM, Quarta C	Prevalence and Incidence of ATTR Amyloidosis in the United States: Insights from Claims Database and Electronic Health Records	Date: Tuesday, May 28 Abstract ID: 68
Laires PA, Zhang Y, Manwani R, Silva AM, Catini J, Thompson J, Dozier M, Yang F	Subtype Distribution of Amyloidosis in the United States: Insights from an Electronic Health Records Database Analysis	Date: Tuesday, May 28 Abstract ID: 112

The full list of ISA 2024 congress abstracts are available online.

INDICATION for WAINUA[TM] (eplontersen)

WAINUA injection, for subcutaneous use, 45 mg is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

IMPORTANT SAFETY INFORMATION for WAINUA[TM] (eplontersen)

WARNINGS AND PRECAUTIONS

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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 US Full Prescribing Information for WAINUA.

Notes

NEURO-TTRansform
NEURO-TTRansform is a global, open-label, randomized trial evaluating the efficacy and safety of eplontersen in patients with hATTR-PN.[8,9] The trial enrolled adult patients with hATTR-PN Stage 1 or Stage 2 compared to the external placebo group from the NEURO-TTR registrational trial that Ionis completed in 2017.[8,9] The comparison of efficacy and safety for WAINUA versus external placebo was based on data up to week 66, and all patients were followed on treatment until week 85, when they had the option to transition into an open-label extension study, which is still ongoing.[8,9]

WAINUA
WAINUA[TM] (eplontersen) is a ligand-conjugated antisense oligonucleotide (LICA) medicine designed to reduce the production of transthyretin, or TTR protein.[9,10] WAINUA has been approved in the US for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults (also referred to as hATTR-PN).[1]

AstraZeneca in amyloidosis
Amyloidosis is a group of complex rare diseases caused by abnormal proteins that misfold and clump together to form toxic amyloids that deposit in tissues or organs, including the heart, kidneys and peripheral nerves.[11-12] The build-up of these toxic amyloids can result in significant organ damage and organ failure that can severely impact quality of life and ultimately be fatal.[11-12] AstraZeneca and its Rare Disease Unit, Alexion, are developing and evaluating multiple modalities with the potential to halt and reduce organ damage across various types of amyloidosis. The Company is uniquely positioned to lead therapeutic and diagnostic advances for people living with amyloidosis with the largest and fastest-growing pipeline of investigational amyloidosis therapies to address the spectrum of patient needs.

Alexion
Alexion, AstraZeneca Rare Disease, is focused on serving patients and families affected by rare diseases and devastating conditions through the discovery, development and delivery of life-changing medicines. A pioneering leader in rare disease for more than three decades, Alexion was the first to translate the complex biology of the complement system into transformative medicines, and today it continues to build a diversified pipeline across disease areas with significant unmet need, using an array of innovative modalities. As part of AstraZeneca, Alexion is continually expanding its global geographic footprint to serve more rare disease patients around the world. It is headquartered in Boston, MA, US.

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US-89473 Last Updated 5/24

About AstraZeneca

AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialization of prescription medicines in Oncology, Rare Diseases and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca operates in over 100 countries, and its innovative medicines are used by millions of patients worldwide. For more information, please visit www.astrazeneca-us.com and follow us on social media @AstraZeneca.

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