Press release
Valby, 2 October, 2025

Lundbeck to showcase amlenetug Phase 3 MASCOT trial design in Multiple System Atrophy at the International Congress of Parkinson's Disease and Movement Disorders® 2025

- Details of the Phase 3 MASCOT trial investigating amlenetug for the treatment of patients with Multiple System Atrophy (MSA) will be presented at the International Congress of Parkinson's Disease and Movement Disorders® 2025[1-3]
- MSA is a rare, rapidly progressing, neurodegenerative disease with no approved treatments available[4,5]
- The innovative design of the pivotal MASCOT trial aims to accelerate drug development for patients living with MSA[1]
- Amlenetug has previously received Orphan Drug Designation (ODD) from the US FDA and the EMA in Europe, in addition to SAKIGAKE designation in Japan

Valby, Denmark, 2 October 2025 – H. Lundbeck A/S (Lundbeck) today announced that pipeline developments regarding amlenetug, a novel investigational molecule for the potential treatment of Multiple System Atrophy (MSA), will be presented at the 2025 International Congress of Parkinson's Disease and Movement Disorders® in Honolulu, Hawaii (Oct 5-9).

Amlenetug is a human monoclonal antibody (mAb), which binds to pathological aggregations of the protein α-synuclein in the brain, thereby inhibiting its spreading to nearby brain cells. Amlenetug holds promise as a first-in-class therapy, with the potential to slow clinical disease progression for patients with MSA, a condition for which no approved treatments currently exist.

At the congress, Lundbeck will share Insights into the design of the Phase 3 MASCOT trial and its use of innovative Bayesian progression modeling methods.[1,2] Rare diseases, such as MSA, face unique challenges due to limited prior data available to guide the design of drug development programs and smaller patient populations to enroll in trials.[6,7]

"MSA is a neurodegenerative disease with no currently available treatments to slow its relentless progression," said Johan Luthman, EVP and Head of Research and Development at Lundbeck. "Amlenetug seeks to address this unmet need by targeting the underlying biology of MSA and delaying disease progression. The MASCOT trial has therefore been designed based on innovative methodologies, including Bayesian progression modeling and adaptive elements, to effectively evaluate its impact on this debilitating neurological disorder."

This dynamic approach utilizes all available data over a long treatment period, enabling assessment of potential slowing of clinical disease progression overall. This is in contrast to traditional clinical trial design, which focuses on isolated time points.

The MASCOT trial[8] is ongoing in many regions, including the EU, US and Japan, where the Bayesian progression modelling framework has been discussed with regulatory authorities in support of marketing registration. This further underscores the innovative nature of Lundbeck's approach and the critical unmet need in this disease area.

During the congress, Lundbeck will also showcase valuable insights from patients and caregivers who participated in the Phase 2 AMULET trial. These perspectives, captured through embedded patient experience interviews, have been instrumental in informing the design of the Phase 3 MASCOT trial and in shedding light on the substantial burden the disease places on patients and their families.[3]

Lundbeck's scientific presentations at the 2025 International Congress of Parkinson's Disease and Movement Disorders®:

Exploring MSA: Bridging clinical insight, experiences of people living with MSA, and the path toward targeted treatment	Scientific Symposium	Wednesday, Oct 8 11:45-12:45 HST
A randomized, double-blind phase 3 trial of amlenetug versus placebo in patients with MSA: The MASCOT study[1]	ePoster Lotte Kjærsgaard	Sunday, Oct 5 12:48 HST
Assessing disease progression in MSA: Development of a Bayesian Progression Model (BPM)[2]	ePoster Jonas Wiedemann	Sunday, Oct 5 13:21 HST
Incorporating patient and care partner feedback on the protocol for a clinical trial assessing progression in MSA[3]	ePoster Beatrice Yang	Sunday, Oct 5 12:57 HST

About Multiple System Atrophy

MSA is a rapidly progressing rare condition that causes damage to nerve cells in the brain. MSA is seriously debilitating and places a high disease burden on patients. Symptoms of MSA usually start between 55 and 60 years of age, and patients typically live for 6 to 9 years after symptom onset.[9]

In a person with MSA, an abnormal build-up of the protein α-synuclein is thought to be responsible for damaging the areas of the brain that control balance, movement, and the body's normal functions.[10] The symptoms of MSA are wide-ranging and include muscle control problems, similar to those of Parkinson's disease.[9] Many different functions of the body can be affected, and symptoms including urinary incontinence, frequent falling, and unintelligible speech occur within 3 years of disease onset and are accompanied by reduced capacity to live independently. Death is often due to respiratory problems. Although there are many different possible symptoms of MSA, not everyone who is affected will experience all of them. There is currently no cure for MSA and no available treatment to slow its progression.[9]

About amlenetug

Amlenetug is a human monoclonal antibody (mAb) that recognizes and binds to all major forms of extracellular α-synuclein and thereby intended to prevent uptake and inhibit seeding of aggregation. Amlenetug is being developed by Lundbeck under a joint research and licensing agreement between Lundbeck and Genmab A/S. Amlenetug is an investigational compound

that is not approved for marketing by any regulatory authority worldwide, and the efficacy and safety of amlenetug have not been established.

About the MASCOT trial

MASCOT (NCT06706622) is a Phase 3 interventional, randomized, double-blind, parallel-group, placebo-controlled, optional open-label extension trial that will be conducted in North America, Europe, Asia and Australia.[8]

The trial comprises 2 parts: A double-blind period where participants are randomized to receive either high or low doses of amlenetug, or placebo for 72 weeks, followed by an open-label extension period where all participants enrolled in the trial are offered treatment with amlenetug. The aim of the trial is to evaluate the efficacy, safety, and tolerability of amlenetug in patients with MSA. Amlenetug will be delivered as an intravenous infusion every four weeks.

About the AMULET trial

AMULET trial (NCT05104476) was a Phase 2, randomized, double-blind, placebo-controlled clinical trial of amlenetug as a potential treatment for patients with MSA. MSA patients were randomized 2:1 to either amlenetug or placebo and treated between 48 to 72 weeks, followed by an ongoing 192 weeks open-label extension period offering all participants to receive treatment with amlenetug.

The primary objective was to evaluate the efficacy of amlenetug on clinical progression in patients with MSA, aiming at showing a slowing in clinical progression in the active treatment arm compared to placebo on a 5% significance level evaluated 1-sided as well as safety and tolerability. The secondary objectives included evaluation of amlenetug on patient's functioning, disease severity and other aspects of MSA. Amlenetug was delivered as an intravenous infusion every four weeks.

Contacts

Anders Crillesen
Head of Media Relations, Corp. Communication
AECE@lundbeck.com
+45 27 79 12 86

Jens Høyer
Vice President, Head of Investor Relations
JSHR@lundbeck.com
+45 30 83 45 01

About H. Lundbeck A/S

Lundbeck is a biopharmaceutical company focusing exclusively on brain health. With more than 70 years of experience in neuroscience, we are committed to improving the lives of people with neurological and psychiatric diseases.

Brain disorders affect a large part of the world's population, and the effects are felt throughout society. With the rapidly improving understanding of the biology of the brain, we hold ourselves accountable for advancing brain health by curiously exploring new opportunities for treatments. As a focused innovator, we strive for our research and development programs to tackle some of the most complex neurological challenges. We develop transformative medicines targeting people for whom there are few or no treatments available, expanding into neuro-specialty and neuro-rare from our strong legacy within psychiatry and neurology.

We are committed to fighting stigma and we act to improve health equity. We strive to create long term value for our shareholders by making a positive contribution to patients, their families and society as a whole.

Lundbeck has approximately 5,700 employees in more than 50 countries and our products are available in more than 80 countries. For additional information, we encourage you to visit our corporate site www.lundbeck.com and connect with us via LinkedIn.

References:

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