

Valby, 14 September 2023

Lundbeck presents clinical advances in migraine prevention with positive trial results at international headache congress

The HOPE trial, together with a clinical mechanism of action study, strengthens the case for Lundbeck's Lu AG09222, as additional data highlights the anti-pituitary adenylate cyclase-activating polypeptide (PACAP) monoclonal antibody (mAb) as a potential preventive treatment for migraine.

H. Lundbeck A/S (Lundbeck) announces new clinical data supporting the efficacy and tolerability of Lu AG09222 for the preventive treatment of migraine at the International Headache Congress (IHC) 2023 in Seoul, Korea.

The presentations also include additional data from a proof-of-mechanism study showing that Lu AG09222 can halt PACAP38-triggered vasodilation and headaches.

Lu AG09222 is an investigational mAb intended to block signals by PACAP. This neuropeptide is believed to contribute to migraine. The data represents the first positive headline results with this mechanism.

Lu AG09222 may offer a potential new treatment option. It aims at a migraine pathway that is distinct from the pathway targeted by the recently introduced anti-calcitonin gene-related peptide (anti-CGRP) treatment approach.

Based on these positive outcomes, Lu AG09222 will progress into further development.

"I am proud to present these data for the first time at a key medical conference. We are committed to advancing novel and effective treatment options for the many patients still suffering from migraine and who are not sufficiently treated by current medications. Lu AG09222 holds a promising position and has a good chance of being a first-in-class with this interesting mechanism," said Johan Luthman, EVP, and Head of Research & Development at Lundbeck.

Scientific presentations from Lundbeck at the IHC

Ashina, M et al. **Efficacy and safety of Lu AG09222 for migraine prevention in patients with 2–4 previous preventive treatment failures: HOPE, an interventional, randomized, double-blind, parallel-group, placebo-controlled Phase 2 trial**

- *HOPE* was an interventional, randomized, double-blind, parallel-group, placebo-controlled Phase 2 trial (NCT05133323), conducted in Georgia, Poland, Czechia, Denmark, and US.

- A total of 237 participants were randomized in this trial (Lu AG09222 high dose, 97; Lu AG09222 low dose, 46; and placebo, 94).
- Participants were 87.8% female with a mean age of 42.5 and 16.7 monthly migraine days (MMDs) at baseline.
- This trial met the primary endpoint; the difference from placebo in mean change in MMDs from baseline over weeks 1-4 was significant with the Lu AG09222 high dose (-2.0 [90%CI -3.5; -0.6]; one-sided p=0.01).
- The change from baseline in mean MMDs was -6.2 (standard error [SE] 0.66) with Lu AG09222 high dose and -4.2 (SE 0.67) with placebo.
- Lu AG09222 was generally well tolerated.

Rasmussen, N et al. **PACAP-targeted antibody Lu AG09222 inhibits vasodilation in healthy volunteers**

- This was an interventional, randomized, double-blind, parallel-group, placebo-controlled, phase 1 trial (NCT04976309).
- Lu AG09222 inhibited PACAP38-induced cephalic vasodilation and increases in heart rate and reduced concomitant headache.

Together, these data support Lu AG09222 as a potential preventive treatment of migraine. They further confirm a role of PACAP in migraine pathophysiology, in addition to the established role of CGRP that is targeted by the current advanced migraine therapies [anti-CGRPs]. With its novel mechanism of action, Lu AG09222 has the potential to help patients with migraine and potentially other pain related indications.

Lundbeck is grateful to all the trial participants, and the investigators who contributed greatly to this research.

About the phase II migraine trial

The HOPE trial was an interventional, multi-national, multi-site, randomized, double-blind, parallel-group, placebo-controlled phase IIa trial designed to assess the safety, tolerability and efficacy of a single intravenous infusion of Lu AG09222 for the prevention of migraine in patients that had failed prior treatments. The trial consisted of a 4-week double-blind treatment period with a follow-up period for 8 weeks. The primary endpoint was the change from baseline in the number of monthly migraine days over weeks 1 to 4, compared to placebo. Secondary endpoints were $\geq 50\%$ reduction from baseline in MMDs (Weeks 1 to 4) and change from baseline in the number of monthly headache days (Weeks 1 to 4), compared to placebo.

The target population for this trial was defined as patients diagnosed with migraine as outlined in the International Classification of Headache Disorders Third Edition (ICHD-3) with unsuccessful prior preventive treatments. A total of 237 patients, recruited from specialist settings, were randomly allocated via a randomization system to one of three treatment groups: two doses of Lu AG09222 or placebo.



About Lu AG09222

Lundbeck is developing Lu AG09222, an investigational mAb designed to bind and inhibit PACAPⁱ. PACAP has emerged as a neuropeptide implicated in the pathophysiology of migraine and represents a novel target in migraine. Lu AG09222 represents a potential new therapeutic option, targeting a pathway in migraine that is distinct from the CGRP pathway that is targeted by the recently available anti-CGRP migraine treatment drug class.

About migraine

Migraine is a complex and incapacitating neurological disease characterized by recurrent episodes of moderate to severe, pulsating headaches typically accompanied by an array of symptoms, including nausea, vomiting, and sensitivity to light and soundⁱⁱ. As the most prevalent neurological disorder in people aged <50 years, migraine imposes both a social and financial burden, affecting around 135 million people in the G7 countries plus China. Repeated migraine attacks, and often the constant fear of the next one, damage family life, social life and work lifeⁱⁱⁱ.

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About H. Lundbeck A/S

Lundbeck is a global pharmaceutical company specialized in brain diseases. For more than 70 years, we have been at the forefront of neuroscience research.

We are tirelessly dedicated to restoring brain health, so every person can be their best. We are committed to fighting stigma and discrimination against people living with brain diseases and advocating for broader social acceptance of people with brain health conditions. Our research programs tackle some of the most complex challenges in neuroscience, and our pipeline is focused on bringing forward transformative treatments for brain diseases for which there are few, if any therapeutic options.

For additional information, we encourage you to visit our corporate site www.lundbeck.com and connect with us via [LinkedIn](#).

ⁱ Moldovan Loomis, C., et al., Pharmacologic Characterization of ALD1910, a Potent Humanized Monoclonal Antibody against the Pituitary Adenylate Cyclase-Activating Peptide. *J Pharmacol Exp Ther*, 2019. 369(1): p. 26-36

ⁱⁱ Headache Classification Committee of the International Headache Society (IHS). *The International Classification of Headache Disorders*, 3rd Edition. Cephalalgia, 2018. 38(1): p. 1-211.

ⁱⁱⁱ Burch, R.C., D.C. Buse, and R.B. Lipton, Migraine: epidemiology, burden, and comorbidity. *Neurol Clin*, 2019. 37(4): p. 631-649.