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Corporate Release

Lundbeck and Otsuka Pharmaceutical announce positive results showing reduced agitation in patients with Alzheimer's dementia treated with brexpiprazole

- *Results from a phase III clinical study for treatment of agitation in patients with Alzheimer's dementia showed that patients treated with brexpiprazole had a statistically significantly greater reduction in agitation compared to placebo*
- *Agitation is a very prevalent clinical manifestation in Alzheimer's dementia and one of the most complex and stressful aspects of care in patients affected by the disease. It is associated with greater caregiver burden, earlier nursing home placement, increased morbidity and mortality and a substantial economic burden.*
- *Currently there are no FDA approved pharmacological treatments for agitation in Alzheimer's dementia*

Valby, Denmark, June 27, 2022 - H. Lundbeck A/S (Lundbeck) and Otsuka Pharmaceutical Co., Ltd. (Otsuka) announce positive results of the phase III clinical trial of brexpiprazole in the treatment of agitation in patients with Alzheimer's dementia (NCT03548584). The analysis concluded that there is a statistically significant difference (p=0.0026) in the mean change from baseline to Week 12 in the Cohen-Mansfield Agitation Inventory (CMAI) total score between brexpiprazole and placebo.

Full study results are not yet available. Further prespecified and exploratory analyses of the data set will be conducted to determine the full potential of brexpiprazole in the treatment of agitation in patients with Alzheimer's dementia.

Based on this outcome Lundbeck and Otsuka are planning a regulatory filing to the FDA later in 2022. The Supplemental New Drug Application will be comprised of this study as well as two earlier trials.[1] In February 2016, the FDA granted fast track designation for brexpiprazole for treatment of agitation in patients with Alzheimer's dementia.

Lundbeck and Otsuka are incredibly grateful to all the patients with Alzheimer´s dementia, their families, caregivers, and the investigators who participated in the trials and contributed greatly to this research.

The trial results are planned to be submitted for scientific publication at a later date.

About the study

Trial 331-14-213 (NCT03548584; Trial 213) was designed to assess the safety, tolerability and efficacy of two fixed doses of brexpiprazole (2 mg/day and 3 mg/day) in the treatment of patients with agitation in Alzheimer's dementia. The trial consisted of a continuous 12-week double-blind treatment period with a 30-

day follow-up. The randomized trial population included 345 male and female patients, aged 55–90 years (inclusive), with a diagnosis of probable Alzheimer's disease, and meeting criteria of agitation as defined by the International Psychogeriatric Association (IPA). The primary outcome was the change in the CMAI total score at week 12 for all patients treated with brexpiprazole versus those treated with placebo. The key secondary outcome was the change in the Clinical Global Impression – Severity of Illness (CGI-S) score, as related to symptoms of agitation. Participating countries include Bulgaria, Hungary, Serbia, Slovakia, Spain, Ukraine, and USA. The study included both patients who were living at home and those living in institutionalized settings.

In the study, the improvements from baseline on the primary endpoint of CMAI for patients receiving brexpiprazole or 2 mg/day or 3 mg/day were statistically greater than for those receiving placebo (p=0.0026). This result was supported by a statistically superior improvement on the key secondary endpoint of CGI-S, as related to agitation (p=0.0055).

Brexpiprazole was generally well tolerated, and no new safety signals were observed. The only Treatment Emergent Adverse Event (TEAE) with more than 5% incidence in patients treated with brexpiprazole was headache (6.6% vs. 6.9% for placebo). The following TEAEs occurred at an incidence of at least 2% in brexpiprazole treatment group and greater than that of placebo: somnolence, nasopharyngitis, dizziness, diarrhea, urinary tract infection, and asthenia. There was one death observed in the 3 mg/day treatment group, assessed as not related to treatment by the investigator.

Conference Call Information

Lundbeck will host a conference call and webcast for investors and analysts today at 10:00 AM CEST to briefly discuss the topline results of the trial. To participate in the live conference call, please use the following dial ins:

Denmark: +45 78768490
United Kingdom: +44 203 7696819
United States: +1 646 787 0157

Pincode for all countries: 930586

To follow the live webcast please use the following link:
https://streams.eventcdn.net/lundbeck/teleconference/

All links and dial ins can also be found on Lundbeck.com

About CMAI

The Cohen-Mansfield Agitation Inventory (CMAI) is a caregiver rated questionnaire that measures the frequency of manifestations of 29 agitated behaviors in elderly persons, such as pacing, restlessness, yelling, and hitting.[2] It has been used extensively for assessing agitation and has been adapted and validated for different patient settings.[2-5]

About agitation in Alzheimer's Dementia

Neuropsychiatric symptoms (NPS) of Alzheimer's dementia, such as agitation are associated with poor caregiver outcomes, including reduced quality of life and poorer health.[6-9]

Agitation is a common neuropsychiatric symptom of Alzheimer's dementia. It is reported in approximately 45% of patients with Alzheimer's dementia and has a large impact on quality of life for the patients and their loved ones.[10-11] It covers a large group of behaviors occurring in patients with Alzheimer's dementia, and it is an excessive/inappropriate manifestation of "normal" human emotions and behaviors. Some behaviors include pacing, gesturing, profanity, shouting, shoving, and hitting.[12]

Symptoms of agitation are also a consistent predictor of nursing home admission in patients with dementia.[13-15]

Agitation in Alzheimer's dementia is thought to be associated with underlying pathophysiological circuit level dysfunctions in noradrenergic, serotonergic, and dopaminergic neurotransmission.[16]

About brexpiprazole

Brexpiprazole was approved in the U.S. on July 10, 2015, as an adjunctive therapy to antidepressants in adults with major depressive disorder and as a treatment in adults with schizophrenia. Brexpiprazole was also approved in 2017 in Health Canada and by the EMA in Europe in 2018 for the treatment of schizophrenia. In addition, brexpiprazole has been approved in several other countries across the world. Brexpiprazole is distributed and marketed under the brand name Rexulti®. In Europe, brexpiprazole is distributed and marketed under the brand name Rxulti®

Brexpiprazole was discovered by Otsuka and is being co-developed by Otsuka and Lundbeck. The efficacy of brexpiprazole may be mediated through a combination of partial agonist activity at noradrenaline alpha1B/2C receptors, serotonin 5-HT1A and dopamine D2 receptors, and antagonist activity at serotonin 5-HT2A receptors, all at pharmacologically relevant potency.[17-18]

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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 on Instagram (h_lundbeck), Twitter at @Lundbeck and via LinkedIn.

Safe Harbor/Forward-Looking Statements

This corporate release contains forward-looking statements that provide our expectations or forecasts of future events such as new product introductions, product approvals and financial performance. Forward looking statements include, without limitation, any statement that may predict, forecast, indicate or imply future results, performance or achievements, and may contain words like "believe", "anticipate", "expect", "estimate", "intend", "plan", "project", "will be", "will continue", "will result", "could", "may", "might", or any variations of such words or other words with similar meanings. All statements other than statements of historical facts included in this presentation, including, without limitation, those regarding our financial position, business strategy, plans and objectives of management for future operations (including development plans and objectives relating to our products), are forward looking statements.

Such forward looking statements involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by such forward looking statements. Factors that may affect future results include, among others, interest rate and currency exchange rate fluctuations, delay or failure of development projects, production or distribution problems, unexpected contract breaches or terminations, government-mandated or market-driven price decreases for Lundbeck's products, introduction of competing products, Lundbeck's ability to successfully market both new and existing products, exposure to product liability and other lawsuits, changes in reimbursement rules and governmental laws and related interpretation thereof, and unexpected growth in costs and expenses.

The forward-looking statements in this document and oral presentations made on behalf of Lundbeck speak only as at the date of this presentation. Lundbeck does not undertake any obligation to update or revise forward-looking statements in this presentation or oral presentations made on behalf of Lundbeck, nor to confirm such statements to reflect subsequent events or circumstances after the date of the presentation or in relation to actual results, unless otherwise required by applicable law or applicable stock exchange regulations.

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