H. Lundbeck A/S

Ottiliavej 9 Tel +45 36 30 13 11 E-mail investor@lundbeck.com
DK-2500 Valby, Copenhagen www.lundbeck.com
CVR number: 56759913
LEI code: 5493006R4KC2OI5D3470

Corporate Release

Lundbeck and Otsuka Pharmaceutical announce topline results from two phase III trials of brexpiprazole as combination therapy with sertraline for the treatment of Post-Traumatic Stress Disorder in adults

- *The flexible dose phase III trial met its primary endpoint, while the fixed dose phase III trial missed its primary endpoint*
- *Lundbeck and Otsuka will discuss these results with FDA to determine next steps*

Valby, Denmark, September 7, 2023 – H. Lundbeck A/S (Lundbeck) and Otsuka Pharmaceutical Co., Ltd. (Otsuka) today announced results from the phase III clinical trials of brexpiprazole as combination therapy with sertraline for the treatment of post-traumatic stress disorder (PTSD) in adults.

The first trial (NCT04124614) was a phase III, randomized, double-blind, 2-arm, flexible dose trial to evaluate the efficacy, safety, and tolerability of brexpiprazole (2 - 3 mg/day) as combination therapy with sertraline in 416 randomized adult subjects with PTSD.

The second trial (NCT04174170) was a phase III, randomized, double-blind, 3-arm, fixed dose trial to evaluate the efficacy, safety, and tolerability of brexpiprazole (2 or 3 mg/day) as combination therapy with sertraline in 553 randomized adult subjects with PTSD.

The primary endpoint for both trials was the change in the Clinician-Administered PTSD Scale (CAPS-5) total score for brexpiprazole + sertraline combination therapy versus sertraline + placebo at week 10 in patients diagnosed with PTSD according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5).

The first trial met its primary endpoint by demonstrating improvements from baseline on the primary endpoint of CAPS-5 for patients receiving brexpiprazole 2-3 mg/day + sertraline combination therapy being statistically significantly greater than for those receiving sertraline + placebo ($p<0.05$). The second phase 3 trial missed its primary endpoint ($p>0.05$).

Overall, the safety and tolerability results were consistent with the profile of brexpiprazole as observed in the clinical trials for schizophrenia, agitation associated with dementia due to Alzheimer's disease (AADAD), and adjunctive treatment of major depressive disorder (MDD). The most common treatment emergent adverse events in patients receiving combination therapy of brexpiprazole + sertraline versus sertraline + placebo (incidence at least 2% and greater than sertraline + placebo) were dyspepsia, fatigue, weight increased, akathisia and somnolence. Discontinuations due to adverse events occurred in 3.7% of patients treated with brexpiprazole + sertraline combination therapy and 7.6% of patients receiving sertraline + placebo.

Full trial results are not yet available. Further prespecified and exploratory analyses of this data set will be conducted to further assess brexpiprazole as combination therapy with sertraline for the treatment of PTSD. The trial results are planned to be submitted for scientific publication.

"The results from the first trial indicate that brexpiprazole in combination with sertraline provides improvement of symptoms for people living with PTSD, whereas the second trial did not meet its primary endpoint," said John Kraus, M.D., Ph.D., executive vice president and chief medical officer, Otsuka Pharmaceutical Development & Commercialization, Inc. *"We will fully analyze these results and will discuss our findings with the FDA to determine next steps."*

"PTSD is a serious mental health disorder with a wide range of symptoms with no new therapeutic options in more than 20 years," Dr. Johan Luthman, executive vice president and head of Research & Development at Lundbeck. *"The two trials constitute one of the largest clinical development programs ever conducted in PTSD. We will analyze the dataset to further determine the potential of brexpiprazole as combination therapy with sertraline in comprehensively addressing symptoms across the PTSD core domains."*

Lundbeck and Otsuka are incredibly appreciative to all the patients with PTSD, their families, and the investigators who participated in the trials and contributed greatly to this research.

About the trials

Trials 331-201-00071 (NCT04124614) and 331-201-00072 (NCT04174170) were designed to evaluate the efficacy, safety and tolerability of brexpiprazole and sertraline combination treatment in adults with PTSD. The trial populations included male and female patients, aged 18-65 years (inclusive), with a diagnosis of PTSD according to the DSM-5 and confirmed by the Mini International Neuropsychiatric Interview. The trials consisted of a 1-week double-blind placebo run-in period followed by 11-weeks of double-blind randomized treatment for a continuous 12-week double-blind treatment period with a 21-day follow-up]. Trial 331-201-00071 was a 2-arm, double-blind, flexible-dose trial in which patients were randomized to receive either flexible-dose brexpiprazole 2-3 mg/day plus sertraline 150 mg/day or sertraline 150 mg/day plus placebo during the 11-week randomized treatment period. Trial 331-201-00072 was a 3-arm, double-blind, fixed-dose trial in which patients were randomized to receive either fixed-dose brexpiprazole 2 mg/day plus sertraline 150 mg/day, brexpiprazole 3 mg/day plus sertraline 150 mg/day, or sertraline 150 mg/day plus placebo during the 11-week randomized treatment period. The primary outcome in both trials was the change from randomization to week 10 in the CAPS-5 total score in those patients that met blinded criteria at the week 1 visit of the trial.

About CAPS-5

The Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) is a structured interview designed to assess PTSD diagnostic status and symptoms severity as defined by the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5). The interview consists of 30 items, with a higher score indicating a worse outcome.

About Post-Traumatic Stress Disorder

PTSD is a psychiatric disorder that may occur in people who have experienced, or witnessed, a traumatic event, series of events or set of circumstances. An individual may experience this as emotionally or physically harmful or life-threatening and may affect mental, physical, social, and/or spiritual well-being.[1]

Examples include natural disasters, serious accidents, terrorist acts, war/combat, rape/sexual assault, historical trauma, intimate partner violence and bullying.[1]

PTSD can occur in all people, of any ethnicity, nationality or culture, and at any age. It affects more than 13 million people in the U.S. and nearly 6 in 100 people will be diagnosed with PTSD in their lifetime.[2] Women are twice as likely as men to have PTSD.[1]

Symptoms of PTSD are generally grouped into four types: intrusive memories, avoidance, negative changes in thinking and mood, and changes in physical and emotional reactions. Symptoms can vary over time or vary from person to person.[3] Symptoms usually begin within 3 months of the traumatic incident, but they sometimes emerge later.[4] To meet the criteria for PTSD, symptoms must last longer than 1 month, and they must be severe enough to interfere with aspects of daily life, such as relationships or work.[4]

About brexpiprazole

Brexpiprazole was approved in the U.S. in 2015, as an adjunctive therapy to antidepressants in adults with MDD and as a treatment for schizophrenia in adults. Most recently, brexpiprazole was approved in the U.S. for the treatment of AADAD in May 2023. Brexpiprazole was also approved by Health Canada for schizophrenia and adjunctive treatment of MDD in 2017 and 2019, respectively. It was approved by the Ministry of Health, Labour and Welfare in Japan and by the European Medicines Agency in 2018 for the treatment of schizophrenia.

Brexpiprazole was discovered by Otsuka and is being co-developed by Otsuka and Lundbeck. The mechanism of action of brexpiprazole is unknown, however the efficacy of brexpiprazole may be mediated through a combination of partial agonist activity at serotonin 5-HT1A and dopamine D2 receptors, antagonist activity at serotonin 5-HT2A receptors, as well as antagonism of alpha 1B/2C receptors.

Lundbeck contacts

Investors:
Palle Holm Olesen
Vice President, Investor Relations
PALO@lundbeck.com
+45 30 83 24 26

Sophia Nørskov-Erichsen
Senior Manager, Investor Relations
SONQ@lundbeck.com
+45 30 83 24 60

Media:
Thomas Mikkel Mortensen
Media Relations Lead, Corp. Communication
THMR@lundbeck.com
+45 30 83 30 24

Otsuka contacts

Otsuka in Japan:
Jeffrey Gilbert (Outside the U.S.)
Leader, Pharmaceutical PR
Otsuka Pharmaceutical Co., Ltd.
gilbert.jeffrey@otsuka.co.jp
+81 3 6361 7379

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.

About Otsuka

Otsuka Pharmaceutical Co., Ltd. is a global healthcare company with the corporate philosophy: Otsuka–people creating new products for better health worldwide. Otsuka researches, develops, manufactures, and markets innovative products, with a focus on pharmaceutical products to meet unmet medical needs and nutraceutical products for the maintenance of everyday health.

In pharmaceuticals, Otsuka is a leader in the challenging areas of mental, renal, and cardiovascular health and has additional research programs in oncology and on several under-addressed diseases including tuberculosis, a significant global public health issue. These commitments illustrate how Otsuka is a “big venture” company at heart, applying a youthful spirit of creativity in everything it does.

Otsuka established a presence in the U.S. in 1973 and today its U.S. affiliates include Otsuka Pharmaceutical Development & Commercialization, Inc. (OPDC) and Otsuka America Pharmaceutical, Inc. (OAPI). These two companies’ 2,000 employees in the U.S. develop and commercialize medicines in the areas of mental health and nephrology, using cutting-edge technology to address unmet healthcare needs.

OPDC and OAPI are indirect subsidiaries of Otsuka Pharmaceutical Company, Ltd., which is a subsidiary of Otsuka Holdings Co., Ltd. headquartered in Tokyo, Japan. The Otsuka group of companies employed 47,000 people worldwide and had consolidated sales of approximately USD 13.1 billion in 2022.

All Otsuka stories start by taking the road less traveled. Learn more about Otsuka in the U.S. at www.otsuka-us.com and connect with us on LinkedIn and X at @OtsukaUS. Otsuka Pharmaceutical Co., Ltd.'s global website is accessible at https://www.otsuka.co.jp/en/.

Citations

1. American Psychiatric Association. What is Posttraumatic Stress Disorder (PTSD). https://www.psychiatry.org/patients-families/ptsd/what-is-ptsd
2. U.S. Department of Veteran Affairs. PTSD: National Center for PTSD. https://www.ptsd.va.gov/understand/common/common_adults.asp
3. Mayo Clinic. Post-traumatic stress disorder (PTSD). https://www.mayoclinic.org/diseases-conditions/posttraumatic-stress-disorder/symptoms-causes/syc-20355967
4. National Institute of Mental Health. Post-Traumatic Stress Disorder. https://www.nimh.nih.gov/health/publications/post-traumatic-stress-disorder-ptsd

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.