CORPORATE RELEASE
Valby, Denmark, 20 September, 2025

Otsuka and Lundbeck receive Complete Response Letter from U.S. FDA for sNDA of REXULTI® (brexpiprazole) in combination with sertraline for the treatment of adults with PTSD

Valby, Denmark, 20 September 2025 - H. Lundbeck A/S (Lundbeck) and Otsuka America Pharmaceutical, Inc., (Otsuka) announce that Otsuka has received a Complete Response Letter (CRL) from the U.S. Food and Drug Administration (FDA) regarding the supplemental New Drug Application (sNDA) for use of REXULTI® (brexpiprazole) in combination with sertraline as a treatment of adults with post-traumatic stress disorder (PTSD). The CRL states that the FDA has completed their review but cannot approve the application in the current form, as the application does not provide substantial evidence of effectiveness to support the approval.

The sNDA for brexpiprazole in combination with sertraline for the treatment of adults with PTSD was accepted for review by the FDA in June 2024 and was based on data from three randomized clinical trials that evaluated the safety and efficacy of brexpiprazole in combination with sertraline in adult patients with PTSD.

The FDA decision follows the Psychopharmacologic Drugs Advisory Committee Meeting on July 18, 2025. The committee voted 1-10 determining that the efficacy of brexpiprazole, when initiated concurrently with sertraline, has not been established for the treatment of PTSD based on the available data presented. Although data from three clinical studies were submitted, the FDA stated in the CRL that not all of these studies are capable of contributing to the substantial evidence of the submission and should Otsuka and Lundbeck be interested in proceeding with the indication, additional positive, adequate and well-controlled trials would be needed to provide substantial evidence of effectiveness.

"While we respect the FDA's decision, we continue to believe in the potential of REXULTI in combination with sertraline to help address this serious unmet need," said John Kraus, M.D., Ph.D., executive vice president and chief medical officer at Otsuka. "Otsuka and Lundbeck will take time to review the contents of the letter with the FDA to determine the appropriate path forward."

Johan Luthman, executive vice president of Lundbeck Research & Development, commented. "Post-traumatic stress disorder places a significant and often overlooked burden on patients, their families, and society. We are grateful to the participants, their families, the clinical trial site investigators and staff, and the entire program team for their dedication and commitment to advancing care for those living with PTSD."

This Corporate Release contains inside information and is disclosed in accordance with Article 17 of the Market Abuse Regulation (EU, no. 596/2014).

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About Post-Traumatic Stress Disorder
PTSD is one of the most common mental health disorders in the United States, with approximately five percent of the population affected during a given year.[i, ii, iii, iv] Most patients (>80%) with PTSD in the United States are in the civilian population.[v, vi] It may occur in people who have experienced or witnessed a traumatic event, series of events or set of circumstances. An individual may experience an event that is emotionally or physically harmful or life-threatening and which may affect mental, physical, social, and/or spiritual well-being. Examples of traumatic events include physical/sexual assault, serious accidents, war/combat, natural disasters, terrorist acts, historical trauma, intimate partner violence and bullying.[vii, viii]

Symptoms of PTSD are generally grouped into four symptom clusters: intrusion (re-experiencing), avoidance, negative cognitions and mood, and marked alterations in arousal and reactivity.[ix] Individual symptom type and intensity can fluctuate over time and between individuals. The average time from index trauma to symptom presentation is typically 2.2 years, and the average time from index trauma to PTSD diagnosis is typically 8.7 years. To meet the criteria for PTSD diagnosis, symptoms must last longer than one month, and they must be severe enough to interfere with aspects of daily life, such as relationships or work. Symptoms also must not be due to medications, substance use, or another medical condition. Guideline-recommended first-line treatment includes psychotherapy (e.g., trauma-focused cognitive behavioral and processing therapy). Pharmacotherapy with certain antidepressants is recommended when these trauma-focused psychotherapies are not available or feasible when patients prefer medications.[x]

About brexpiprazole
Brexpiprazole was approved in the U.S. by the FDA in 2015, as an adjunctive therapy to antidepressants in adults with major depressive disorder (MDD) and as a treatment for schizophrenia in adults. Most recently, brexpiprazole was approved in the U.S. for the treatment of agitation associated with dementia due to Alzheimer's disease, in May 2023. Brexpiprazole has also been approved in more than 60 countries worldwide, including the European Union, Canada and Japan.

Brexpiprazole was discovered by Otsuka and is being co-developed by Otsuka and Lundbeck. The mechanism of action of brexpiprazole is unknown. Brexpiprazole has high receptor binding affinity to norepinephrine, serotonin and dopamine receptors. It is an antagonist at norepinephrine α1B and α2C receptors and serotonin 5-HT2A receptors, as well as a partial agonist at serotonin 5-HT1A and dopamine D2 receptors.[xi, xii]

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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 5,500 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.

About Otsuka

Otsuka Pharmaceutical Co., Ltd. is a total healthcare company that focuses on each individual's potential to enhance their well-being. Our medical-related business provides treatments and diagnostics for both physical and mental health. Our nutraceutical business supports daily health maintenance and improvement. Otsuka's unique products and services are based on scientific evidence, under the guidance of our corporate philosophy: Otsuka-people creating new products for better health worldwide.

Otsuka established a presence in the U.S. in 1973 and today our U.S. affiliates include Otsuka Pharmaceutical Development & Commercialization, Inc. (OPDC) and Otsuka America Pharmaceutical, Inc. (OAPI). These two companies' 2,250 employees 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 Co., Ltd., which is a subsidiary of Otsuka Holdings Co., Ltd. headquartered in Tokyo, Japan. The Otsuka group of companies employed 35,340 people worldwide and had consolidated sales of approximately USD 14.7 billion in 2024.
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 Twitter at @OtsukaUS. Otsuka Pharmaceutical Co., Ltd.'s global website is accessible at https://www.otsuka.co.jp/en/.

Citations

[i] Kessler RC, Petukhova M, Sampson NA, Zaslavsky AM, Wittchen H -U. Twelve-month and lifetime prevalence and lifetime morbid risk of anxiety and mood disorders in the United States. Int J Methods Psychiatr Res. 2012;21(3):169-184.

[ii] Lehavot K, Katon JG, Chen JA, Fortney JC, Simpson TL. Post-traumatic Stress Disorder by Gender and Veteran Status [published correction appears in Am J Prev Med. 2019 Oct;57(4):573]. Am J Prev Med. 2018;54(1):e1-e9.

[iii] Lancaster CL, Teeters JB, Gros DF, Back SE. Posttraumatic Stress Disorder: Overview of Evidence-Based Assessment and Treatment. J Clin Med. 2016;5(11):105.

[iv] U.S. Department of Veterans Affairs. How Common Is PTSD in Adults? Last updated: Feb. 3, 2023. Last accessed: April 30, 2024. Available at: https://www.ptsd.va.gov/understand/common/common_adults.asp

[v] Davis LL, Schein J, Cloutier M, et al. The Economic Burden of Posttraumatic Stress Disorder in the United States From a Societal Perspective. J Clin Psychiatry. 2022;83(3):21m14116.

[vi] Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication [published correction appears in Arch Gen Psychiatry. 2005 Jul;62(7):768. Merikangas, Kathleen R [added]]. Arch Gen Psychiatry. 2005;62(6):593-602.

[vii] American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Arlington, VA, American Psychiatric Association, 2013

[viii] American Psychiatric Association. What is Posttraumatic Stress Disorder (PTSD)? Last updated: November 2022. Last accessed: August 28, 2024. Available at: https://www.psychiatry.org/patients-families/ptsd/what-is-ptsd.

[ix] Wang PS, Berglund P, Olfson M, Pincus HA, Wells KB, Kessler RC. Failure and delay in initial treatment contact after first onset of mental disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry. 2005;62(6):603-613.

[x] U.S. Department of Veterans Affairs. VA/DoD Clinical Practice Guidelines. Management of Posttraumatic Stress Disorder and Acute Stress Disorder. Provider Summary 2023. Version 4.0. www.healthquality.va.gov/guidelines/MH/ptsd/VA-DoD-CPG-PTSD-Provider-Summary.pdf

[xi] REXULTI® (brexpiprazole). Prescribing Information. FDA.

[xii] Maeda K, Sugino H, Akazawa H, et al. Brexpiprazole I: in vitro and in vivo characterization of a novel serotonin-dopamine activity modulator. J Pharmacol Exp Ther. 2014;350(3):589-604.

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 document. 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.