Press release
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Otsuka and Lundbeck Issue Statement on U.S. Food and Drug Administration (FDA) Advisory Committee Meeting on REXULTI in Combination with Sertraline for the Treatment of Post-Traumatic Stress Disorder (PTSD)

Valby, Denmark, 18 July 2025 – Otsuka Pharmaceutical Development & Commercialization, Inc. (Otsuka) and Lundbeck LLC (Lundbeck) announce that the Psychopharmacologic Drugs Advisory Committee (PDAC) of the U.S. Food and Drug Administration (FDA) met to discuss the supplemental New Drug Application (sNDA) of Rexulti® (brexpiprazole) in combination with sertraline for the treatment of adults with post-traumatic stress disorder (PTSD). The committee voted 1-10, concluding 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. The feedback from the committee will be taken into consideration by the FDA as it reviews the application for brexpiprazole in combination with sertraline for the treatment of adults with post-traumatic stress disorder (PTSD).

“Although today’s outcome was disappointing, we remain fully committed to collaborating with the FDA as they complete their review of this application,” said John Kraus, M.D., Ph.D., executive vice president and chief medical officer, Otsuka. “We continue to believe in brexpiprazole’s potential to make a meaningful difference as a treatment option for the PTSD patient population.”

The sNDA is based on previously disclosed data from two Phase 3 trials (NCT04124614 – flexible-dose trial, n=416 and NCT04174170 – fixed-dose trial, n=553), and one Phase 2 trial (NCT03033069 –flexible-dose trial, n=321). All three trials investigated the treatment of PTSD in adults treated with brexpiprazole in combination with sertraline versus sertraline plus placebo.

“Our dedication to patients and the broader PTSD community remains unwavering,” said Johan Luthman, executive vice president of Lundbeck Research & Development. “PTSD has long been a complex condition to treat, and we thank the patients, investigation sites and everyone who participated in the clinical trials.”

Otsuka and Lundbeck will continue to work closely with the FDA as it completes its review of the application.

About Post-Traumatic Stress Disorder

PTSD is one of the most common mental health disorders in the United States, impacting an estimated 13 million adults each year[1-4]. Most patients (86%) with PTSD in the United States are in the civilian population[5,6]. 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, natural disasters, serious accidents, terrorist acts, war/combat, historical trauma, intimate partner violence and bullying[7,8].

Symptoms of PTSD are generally grouped into four symptom clusters: intrusion (re-experiencing), avoidance, negative alterations in mood and cognition, and arousal[9]. 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., cognitive behavioral therapy) and first line pharmacotherapy options include certain antidepressants[10].

About Brexpiprazole

Brexpiprazole was approved in the U.S. by 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 was also approved by Health Canada for schizophrenia and adjunctive treatment of MDD in 2017 and 2019, respectively, and for symptomatic management of agitation associated with Alzheimer's dementia (AAD) in patients with aggressive behavior, unresponsive to non-pharmacological approaches in 2024. It was approved by the European Medicines Agency in 2018 for the treatment of schizophrenia and the Ministry of Health, Labour and Welfare in Japan for the treatment of schizophrenia and MDD in 2018 and 2023, respectively. In 2024, Japan's Ministry of Health, Labour and Welfare also approved brexpiprazole for the treatment of excessive motor activity or physically/verbally aggressive behavior due to rapid changes in mood, irritability, and/or outbursts associated with dementia due to Alzheimer's disease.

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[11,12].

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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 5,700 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.

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