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Otsuka and Lundbeck Issue Statement on U.S. Food and Drug Administration (FDA) Advisory Committee Meeting on brexpiprazole for the Treatment of Agitation Associated with Alzheimer's Dementia

Otsuka Pharmaceutical Co., Ltd. (Otsuka) and H. Lundbeck A/S (Lundbeck) announce the Joint Meeting of the Psychopharmacologic Drugs Advisory Committee and the Peripheral and Central Nervous System Drugs Advisory Committee of the U.S. Food and Drug Administration (FDA) met to discuss the supplemental New Drug Application (sNDA) of REXULTI® (brexpiprazole) for the treatment of agitation associated with Alzheimer's dementia (AAD). The committee voted 9-1 that Otsuka and Lundbeck provided sufficient data to allow the identification of a population in whom the benefits of treating AAD with brexpiprazole outweigh its risks.

If approved, brexpiprazole would be the first FDA-approved treatment indicated for AAD in the U.S. The FDA will consider the feedback from the committee as it reviews the sNDA for brexpiprazole in advance of the May 10 Prescription Drug User Fee Act (PDUFA) target action date.

"We are thankful to the FDA and committee members for the thoughtful review and discussion of brexpiprazole for the treatment of agitation associated with Alzheimer's dementia," said John Kraus, M.D., Ph.D., executive vice president and chief medical officer at Otsuka. "We will continue to work closely with the FDA in advance of our scheduled PDUFA date and feel confident in the impact brexpiprazole could have in addressing the significant unmet need within the Alzheimer's community."

The sNDA included data from two positive clinical phase III studies that investigated the treatment of brexpiprazole in patients with AAD. Study 331-12-283 demonstrated brexpiprazole 2 mg/day was statistically superior to placebo for the primary endpoint of mean change in Cohen-Mansfield Agitation Inventory (CMAI) Total Score from baseline to Week 12 ($p < 0.05$). In Study 331-14-213, treatment with brexpiprazole 2 and 3 mg/day showed statistically significant improvement compared with placebo for the primary efficacy endpoint, the mean change in CMAI Total Score from baseline to Week 12 ($p < 0.05$).

"Agitation is one of the most complex and stressful aspects of care in patients affected by Alzheimer's dementia," said Johan Luthman, executive vice president, Lundbeck Research & Development. "With no FDA-approved products for AAD, there is an urgent need for a treatment that could lessen the neuropsychiatric symptoms that AAD patients and caregivers struggle with. Having an approved treatment option for AAD could provide hope to people

impacted by this debilitating condition."

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.[1-4]

Agitation is a common neuropsychiatric symptom of Alzheimer's dementia. It is reported in approximately 45 percent of patients with Alzheimer's dementia and has a large impact on quality of life for the patients, family members, and caregivers.[5-6] Agitation 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. Such behaviors include pacing, gesturing, profanity, shouting, shoving, and hitting.[7]

Symptoms of agitation are also a consistent predictor of nursing home admission in patients with dementia.[8-10]

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 for schizophrenia in adults. Brexpiprazole was also approved in 2017 in Health Canada and by the EMA in Europe 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 and antagonism at noradrenaline alpha1B/2C receptors and at serotonin 5-HT2A receptors. In addition, brexpiprazole is an antagonist at noradrenaline alpha 1a, 1b, 1d and 2c receptors and partial agonist activity at serotonin5-HT1A and dopamine D2 receptors all at pharmacologically relevant potencies.[11-12]

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