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Otsuka and Lundbeck to Start Third Phase 3 Trial in June to Evaluate Brexpiprazole in the Treatment of Agitation in Patients with Alzheimer's Disease

Otsuka Pharmaceutical Company, Ltd. (Otsuka) and Lundbeck announce that the two companies' third clinical Phase 3 study of brexpiprazole in the treatment of agitation in patients with dementia of the Alzheimer's type will commence in June.

Approximately 300 patients are expected to be enrolled in this 12-week, randomized, double-blind, placebo-controlled trial. Additional information about the trial will be available in the near future at clinicaltrials.gov and will be updated periodically following initiation of the study.

The decision to initiate a third trial follows discussions with the U.S. Food and Drug Administration (FDA) regarding two Phase 3 clinical trials for the agitation in Alzheimer's disease indication that were completed by Otsuka and Lundbeck in 2017. Results for the two completed trials were announced in May of last year and presented in poster sessions at the American Association for Geriatric Psychiatry annual meeting in March of this year.

About Alzheimer's Disease and Related Agitation

Of the approximately 5.5 million people in the U.S. with dementia, it is estimated that 60-80 percent have Alzheimer's disease.[1,2] Behavioral symptoms develop in the majority of people with Alzheimer's disease and many of these symptoms are clinically diagnosed as agitation, including wandering, restlessness, significant emotional distress, aggressive behaviors, and irritability. It is estimated that agitation symptoms affect nearly 50 percent or more of patients with Alzheimer's disease observed over a multiyear period.[3]

Symptoms of agitation place a serious burden on the people afflicted with the disease and their caregivers, significantly affecting the quality of life for all concerned. Agitation is often a determining factor in the decision to place patients in high-level residential care facilities, contributing to the roughly USD 259 billion cost burden of Alzheimer's disease in the U.S. for 2017.[1]

About Brexpiprazole

Brexpiprazole was approved by the U.S. Food and Drug Administration in July 2015 to treat patients with schizophrenia and as an adjunctive treatment for patients with major depressive disorder. Brexpiprazole was subsequently approved in Canada, Australia and Japan for the treatment of schizophrenia. In all four countries brexpiprazole is distributed and marketed under the brand name REXULTI®. Brexpiprazole is not approved for use in treating agitation associated with Alzheimer's disease.

Brexpiprazole was discovered by Otsuka and is being co-developed by Otsuka and Lundbeck. The mechanism of action for brexpiprazole in the adjunctive treatment of major depressive disorder or schizophrenia is not fully understood. However, the efficacy of brexpiprazole may be mediated through a combination of partial agonist activity at serotonin 5-HT_{1A} and dopamine D_2 receptors, and antagonist activity at serotonin 5-HT_{2A} receptors. Brexpiprazole exhibits high affinity (sub-nanomolar) for these receptors as well as for noradrenaline $alpha_{1B/2C}$ receptors.

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[1] Alzheimer's Association. 2017 Alzheimer's disease facts and figures. 2017;13:325-373
[2] Alzheimer's Disease International, The world Alzheimer's report 2015; 30
[3] Bergh, S.and Selbæk, G. The prevalence and the course of neuropsychiatric symptoms in patients with dementia. Norsk Epidemiologi 2012; 22 (2): 225-232.