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Otsuka and Lundbeck report phase III data evaluating brexpiprazole for the treatment of manic episodes associated with bipolar I disorder

- The efficacy of brexpiprazole for the acute treatment of manic episodes, with or without mixed features, in subjects with bipolar I disorder was investigated in two three-week, double-blind, placebo-controlled trials
- The studies did not meet the primary endpoint of statistical separation from placebo as measured by the Young Mania Rating Scale (YMRS) at week 3
- The companies will conduct a thorough analysis of the study results to determine next steps

Otsuka Pharmaceutical Co., Ltd. (Otsuka) and H. Lundbeck A/S (Lundbeck) announce today that data from two global Phase III clinical trials evaluating the safety and efficacy of brexpiprazole for the treatment of patients with manic episodes associated with bipolar I disorder did not meet the primary endpoint. The duration of the randomized phase of each trial was three weeks.

The two multicenter, randomized, double-blind studies of brexpiprazole versus placebo comprised a total of approximately 650 bipolar I patients who experienced an acute manic episode, with or without mixed features, that required hospitalization. The primary efficacy measure to assess the psychiatric signs and symptoms was determined using the Young Mania Rating Scale (YMRS). The YMRS score is a widely-used clinician rating scale to assess mania symptoms based on a patient's subjective reports of their condition and clinical observations made during interviews.

The studies did not meet the primary endpoint of statistical separation from placebo as measured by the Young Mania Rating Scale (YMRS) at week three. In both studies, the placebo effect on the rating scales was substantially higher than anticipated.

Brexpiprazole was generally well tolerated in the trials. The most common adverse reactions observed during the trials were akathisia (6.5%) and headache (5%) and no other adverse events were greater than 3% for patients receiving brexpiprazole across the two studies

The companies will conduct a thorough analysis of the study results to determine next steps. The results from the bipolar I disorder mania studies do not have any bearing on the approved indications of brexpiprazole as treatment for people living with major depressive disorder (MDD) and schizophrenia.

About the Studies

The two trials were multicenter, randomized, double-blind, placebo-controlled phase III studies that enrolled a total of approximately 650 participants. Trial participants had been diagnosed with bipolar I disorder and were between 18 and 65 years of age. Participants had a history of at least one previous acute manic episode, with or without mixed features that required hospitalization or treatment with a mood stabilizer or an antipsychotic agent. Each of the trials studied a starting dose of 2 mg per day and titrated to a maximum of 4 mg per day of brexpiprazole or placebo. These studies were done in multiple centers in North America and Europe.

About Bipolar I Disorder

BP-I is a chronic mental illness with a 12-month and lifetime prevalence in the U.S. of 1.5 percent and 2.1 percent, respectively. People with BP-I experience one or more episodes of mania, and may have episodes of both mania and depression.

About Brexpiprazole

Brexpiprazole is a molecule discovered by Otsuka and co-developed by Otsuka and Lundbeck. The mechanism of action for brexpiprazole in the adjunctive treatment of major depressive disorder or schizophrenia is unknown. However, the efficacy of brexpiprazole may be mediated through a combination of partial agonist activity at serotonin 5-HT_{1A} and dopamine D₂ receptors, and antagonist activity at serotonin 5-HT_{2A} receptors. Brexpiprazole exhibits high affinity (subnanomolar) for these receptors as well as for noradrenaline alpha1B/2C receptors. The drug was approved in the U.S. in July 2015, as an adjunctive therapy to antidepressants in adults with major depressive disorder and as a treatment in adults with schizophrenia. Brexpiprazole was also approved in 2017 by Health Canada and in 2018 by the MHLW in Japan and by the EMA in Europe for the treatment of schizophrenia. In addition, brexpiprazole has been approved in several other countries across the world. Brexpiprazole is distributed and marketed under the brand name Rexulti[®]. In Europe, brexpiprazole is distributed and marketed under the brand name Rxulti[®].

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