RESULTS OF PHASE III STUDY OF BREXPIRAZOLE IN ADULT PATIENTS WITH SCHIZOPHRENA PUBLISHED IN AMERICAN JOURNAL OF PSYCHIATRY

- Brexiprazole demonstrated statistically significant efficacy vs. placebo in PANSS (Positive and Negative Syndrome Scale) Total Score in adult patients with schizophrenia.¹
- Brexiprazole is a serotonin-dopamine activity modulator (SDAM). Brexiprazole is a partial agonist at 5-HT₁A and dopamine D₂ receptors at relatively equal potency, an antagonist at 5-HT₂A and an antagonist at noradrenaline alpha₁B/2C receptors.²
- At least 21 million people in the world are estimated to be affected by schizophrenia, including 2.4 million adults in the U.S.³,⁴

Tokyo, Japan and Deerfield, Ill. – April 17, 2015 – Results from a multicenter study evaluating the effects of the investigational compound brexiprazole, as monotherapy in adult patients with schizophrenia, were published today online by the American Journal of Psychiatry. The study, “Efficacy and Safety of Brexpiprazole for the Treatment of Acute Schizophrenia: A 6-Week, Randomized, Double-Blind, Placebo-Controlled Trial” evaluated the efficacy and tolerability of brexiprazole in adult patients with an acute exacerbation of schizophrenia. The results will be featured in the September 2015 print issue of the publication.

“Schizophrenia is a complicated disease and while advances have been made, patients often still lack an effective treatment path,” said Dr. Christoph U. Correll, Professor of Psychiatry, Hofstra North Shore LIJ School of Medicine and Medical Director, Recognition and Prevention Program (RAP), The Zucker Hillside Hospital, both in New York, and lead investigator of the study. “It is important for clinicians and patients to have a range of treatment options to manage symptoms, and the publication of these data helps increase awareness of the potential of brexiprazole in this patient population.”

Study Results

The Phase III trial randomized 636 patients with acute schizophrenia to fixed doses of brexiprazole (0.25 mg, 2 mg or 4 mg) or placebo (randomized 1:2:2:2), respectively, for 6 weeks.¹ The results indicated that brexiprazole 2 mg and 4 mg demonstrated significant improvement versus placebo in the primary endpoint of change from baseline to Week 6 in PANSS (Positive and Negative Syndrome Scale) Total Score (0.25 mg: -14.90; 2 mg: -20.73, p=0.0001; 4 mg: -19.65, p=0.0006 vs. placebo -12.01).¹

Key secondary endpoint result, the change in CGI-S (Clinical Global Impression-Severity Scale) score at Week 6, supported the primary results (0.25 mg: -0.85; 2 mg: -1.15, p=0.006; 4mg: -1.20, p=0.002 vs. placebo -0.82).¹ Improvements (p<0.05) from baseline to Week 6 in the 2 mg and 4 mg groups compared to placebo were seen in the following secondary efficacy endpoints: PANSS positive and negative subscales, PANSS Excited Component score and PANSS Marder factor scores relating to positive and negative symptoms, disorganized thought and uncontrolled hostility/excitement.¹

Overall, approximately 65% of patients completed the 6-week study.¹ Discontinuations due to adverse events were 13.3%, 8.2%, 9.4%, and 17.4%, while discontinuations due to lack of efficacy were 8.1%, 9.4%, 3.9% and 10.1% in the brexiprazole 0.25 mg, 2 mg, 4 mg and placebo groups, respectively.¹
The most frequently reported treatment-emergent adverse events (TEAEs; greater than 5% in at least one brexpiprazole treatment arm and more frequent than placebo) were diarrhea (5.6%, 1.6%, 3.9% vs. 1.6%), nausea (1.1%, 5.5%, 3.3% vs. 4.3%), akathisia (0%, 4.4%, 7.2% vs. 2.2%) and headache (10.0%, 9.3%, 12.2% vs. 8.2%) in the brexpiprazole 0.25 mg, 2 mg, 4 mg versus placebo groups, respectively. Other activating (restlessness, insomnia, anxiety) and sedating (somnolence, fatigue, sedation) treatment-emergent adverse events were reported with a similar or lower incidence in patients receiving brexpiprazole compared with those receiving placebo. There were no clinically significant effects on low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TG) and total cholesterol (TC).

Otsuka and Lundbeck initially presented results from this pivotal Phase III study evaluating the effects of brexpiprazole as monotherapy in adult patients with schizophrenia at the 53rd Annual Meeting of the American College of Neuropsychopharmacology (ACNP) in December 2014.

About Brexpiprazole (OPC-34712)
Brexipiprazole is a novel investigational psychotropic compound discovered by Otsuka and under co-development with Lundbeck. A New Drug Application for brexpiprazole has been filed with the U.S. Food and Drug Administration (FDA) and the PDUFA date is July 2015 (PDUFA date).

About Schizophrenia
At least 21 million people worldwide are estimated to be affected by schizophrenia, including approximately 2.4 million adults in the U.S. Schizophrenia symptoms usually start to appear between ages 16 and 30.

About Otsuka Pharmaceutical Co., Ltd.
Otsuka Pharmaceutical is a global healthcare company with the corporate philosophy, “Otsuka – people creating new products for better health worldwide.” Otsuka researches, develops, manufactures and markets innovative and original products, with a focus on pharmaceutical products for the treatment of diseases and nutraceutical products for the maintenance of everyday health. In pharmaceuticals, Otsuka is a leader in the challenging area of mental health and also has research programs on several under-addressed diseases including tuberculosis, a significant global public health issue. These commitments illustrate how Otsuka is a “big venture” company at heart, applying a youthful spirit of creativity in everything it does.

Otsuka Pharmaceutical, which employs approximately 28,700 people worldwide, is a wholly owned subsidiary of Otsuka Holdings Co., Ltd., the holding company for the Otsuka Group that is headquartered in Tokyo, Japan. The Otsuka Group has business operations in 26 countries and regions around the world, with consolidated sales of approximately USD 14.1 billion for fiscal year 2013 (4/1/2013-3/31/2014.) Otsuka welcomes you to visit its global website at https://www.otsuka.co.jp/en.

About Lundbeck
Based in Deerfield, Ill., Lundbeck US is an affiliate of H. Lundbeck A/S in Denmark, and focused solely on accelerating therapies for brain disorders. The company is engaged in the research, development, production, marketing and sale of innovative therapies that fulfill unmet medical needs among people living with challenging and sometimes rare neurologic and psychiatric disorders. In its late-stage research pipeline, the company has neurology compounds under investigation for Alzheimer’s disease and epilepsy, in addition to therapies in development for mental health disorders. With a special commitment to the lives of patients, families and caregivers, Lundbeck actively engages in hundreds of initiatives each
year that support our patient communities. To learn more, visit us at www.LundbeckUS.com and connect with us on Twitter at @LundbeckUS.

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2 Maeda, K. et al. Pharmacological Profile of Brexpiprazole (OPC-24712); a Novel Serotonin-Dopamine Activity Modulator.