OTSUKA AND LUNDBECK PRESENT PHASE III DATA ON BREXPIPRAZOLE AS ADJUNCTIVE THERAPY IN ADULT PATIENTS WITH MAJOR DEPRESSION AT THE AMERICAN COLLEGE OF NEUROPSYCHOPHARMACOLOGY ANNUAL MEETING

- Results from two Phase III clinical studies demonstrated the effects of brexpiprazole as adjunctive treatment in patients with major depressive disorder (MDD) who had an inadequate response to monotherapy antidepressant treatments (ADT).
- Brexpiprazole is a serotonin-dopamine activity modulator (SDAM) and is believed to possess a balanced combination of potent activities at multiple receptors in the brain including partial agonist activity at dopamine D_2 and serotonin $5HT_{1A}$ receptors, and antagonist activity at serotonin $5HT_{2A}$ receptors and noradrenergic $alpha_{1B/2C}$ receptors.
- Also being presented at ACNP are results from two Phase III clinical studies of brexpiprazole in adult patients with schizophrenia.

Tokyo, Japan and Valby, Denmark – December 10, 2014 – Otsuka Pharmaceutical Co., Ltd. (Otsuka) and H. Lundbeck A/S (Lundbeck) today announced the presentation of Phase III study results evaluating the efficacy of investigational compound brexpiprazole as adjunctive treatment to antidepressant therapy (ADT) in patients with major depressive disorder (MDD) at the 53rd Annual Meeting of the American College of Neuropsychopharmacology (ACNP) in Phoenix, Arizona. The data were shared in a poster presentation, "Efficacy and Safety of Adjunctive Brexpiprazole (OPC-34712) in Major Depressive Disorder: Results of Two Pivotal Clinical Studies."

"Inadequate response to monotherapy antidepressant treatment is frustrating for patients and the likelihood of remission with multiple lines of therapy decreases substantially with each successive treatment," said Michael E. Thase, MD, Professor of Psychiatry, Director, Mood and Anxiety Program, University of Pennsylvania School of Medicine and study investigator. "These results are very encouraging in that they provide evidence of efficacy and safety of brexpiprazole as an adjunctive treatment to antidepressant therapy in patients with major depressive disorder who had an inadequate response to antidepressant therapy."

MDD Study Results

The poster featured results of two Phase III clinical studies evaluating the efficacy, safety and tolerability of adjunctive brexpiprazole in patients with MDD and inadequate response to ADT (Study 1: NCT01360645; Study 2: NCT01360632). Patients with MDD who failed to reach adequate response during 1-3 treatment attempts with ADT (which is commonly found in current clinical practice) were enrolled and received an additional trial with a (single-blind) ADT for 8 weeks. Those patients who still

failed to reach an adequate response throughout this phase were then randomized (double-blind) to ADT and brexpiprazole or ADT and placebo for 6 weeks. The primary endpoint for both studies was change in MADRS (Montgomery–Åsberg Depression Rating Scale) Total Score from baseline to Week 6. Pre-specified analyses were conducted both on the efficacy population and on the final protocol population (fulfilling amended randomization criteria) for each individual study.

In both studies, key findings included:

- Adjunctive brexpiprazole showed greater improvement than adjunctive placebo in MADRS total score at Week 6 in the efficacy population per final protocol in Study 1 (2mg+ADT [N=175]: -3.21, p=0.0002), and in Study 2 (1mg+ADT [N=211]: -1.30, p=0.0737; 3mg+ADT [N=213]: -1.95, p=0.0079). Similar results were observed for the efficacy population in both studies.
- The completion rate was high (>90%) and comparable across brexpiprazole and placebo groups. Discontinuations due to adverse events were low across all groups (1mg = 1.3%, 2mg = 3.2%, 3mg = 3.5%, placebo = 0.7%) and only one patient discontinued due to lack of efficacy (in the brexpiprazole 1mg group).
- All doses of adjunctive brexpiprazole resulted in notably low levels of sedating or activating side effects.
- The most frequent adverse events (incidence >5% in any group and more than twice the incidence in the placebo group across the two studies) included akathisia (4.4%, 7.4%, 13.5% vs.1.7%), weight increase (6.6%, 8.0%, 5.7% vs. 1.9%), tremor (4.0%, 2.1%, 5.2% vs. 2.2%) somnolence (4.0%, 4.3%, 5.7% vs. 0.5%) and nasopharyngitis (6.6%, 1.1%. 3.1% vs. 1.7%), in the brexpiprazole 1mg+ADT (N=226), 2mg+ADT (N=188), 3mg+ADT (N=229) versus combined placebo + ADT groups (N=411), respectively.

The results from Study 1 were previously presented in a poster session at the 22nd European Psychiatry Association Congress (EPA) in March 2014.

"These results support previously reported data investigating the effect of brexpiprazole for patients with major depressive disorder," said William Carson, MD, CEO, Otsuka Pharmaceutical Development & Commercialization, Inc. "There are more than 14 million adults with this condition in the U.S., of which a significant portion continuously suffer from inadequate response to antidepressant therapy, and new therapeutic options are needed to help those patients struggling to find effective, tolerable treatments. These study results suggest we are on the right track."

"We are committed to patients who suffer from depression," said Anders Gersel Pedersen, MD, EVP and head of R&D in Lundbeck. "We are very grateful to patients, investigators and the broader mental health community for their collaboration and support of our extensive clinical program studying brexpiprazole, and we believe in its potential to make a difference for patients and their families affected by major depressive disorder."

Otsuka and Lundbeck will also present at ACNP Phase III data results evaluating the effect of brexpiprazole as a monotherapy in adult patients with schizophrenia. The data will be shared in two poster presentations, "A Multicenter, Randomized, Controlled, Phase III Trial of Fixed-dose Brexpiprazole for the Treatment of Adults with Acute Schizophrenia" and "Brexpiprazole for the Treatment of Acute Schizophrenia: A Randomized, Controlled Trial."

About Brexpiprazole (OPC-34712)

Brexpiprazole is a novel investigational psychotropic compound discovered by Otsuka and under co-development with Lundbeck. Brexpiprazole is a serotonin-dopamine activity modulator (SDAM) that acts as a partial agonist at 5-HT_{1A} and dopamine D_2 receptors, and an antagonist at 5-HT_{2A} and noradrenaline $alpha_{1B/2C}$ receptors, all with similar high potency (< 1nM). A New Drug Application for brexpiprazole has been filed with the U.S. Food and Drug Administration (FDA) and the PDUFA date is in July 2015.

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 H. Lundbeck A/S

Lundbeck is a global pharmaceutical company highly committed to improving the quality of life of people living with brain diseases. For this purpose, Lundbeck is engaged in the entire value chain throughout research, development, production, marketing and sales of pharmaceuticals across the world. The company's products are targeted at disorders such as depression and anxiety, psychotic disorders, epilepsy, Huntington's, Alzheimer's and Parkinson's diseases. Lundbeck's pipeline consists of several mid- to late- stage development programs.

We have employees in 57 countries, and our products are registered in more than 100 countries. We have research centers in Denmark, China and the United States and production facilities in Italy, France, Mexico, China and Denmark. Lundbeck generated revenue of approximately DKK 15 billion in 2012. For additional information, we encourage you to visit our corporate site www.lundbeck.com.

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