December 10, 2014

For Immediate Release

Company name	Otsuka Holdings Co., Ltd.
Representative	Tatsuo Higuchi President and Representative Director, CEO
Code number	4578 First Section , Tokyo Stock Exchange
Inquiries	Yuji Kogure Director, Investors Relations Department

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

Otsuka Pharmaceutical Co., Ltd., a wholly-owned subsidiary of Otsuka Holdings Co. Ltd., and H. Lundbeck A/S today announced that the presentation of Phase III study results evaluating the efficacy of investigational compound brexpiprazole as adjunctive treatment to antidepressant therapy in patients with major depressive disorder at the 53rd Annual Meeting of the American College of Neuropsychopharmacology in Phoenix, Arizona.

＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊

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).