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Press Release

Valby, December 11, 2014

Otsuka and Lundbeck´s brexpiprazole demonstrates statistically significant effects in New Phase III Studies in adult patients with schizophrenia presented at the American College of Neuropsychopharmacology annual meeting

- *Results from two Phase III clinical studies demonstrated the effects of brexpiprazole in adult patients with schizophrenia.*

- *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 D2 and serotonin 5HT1A receptors, and antagonist activity at serotonin 5HT2A receptors and noradrenergic alpha1B/2C receptors.*

- *Also being presented at ACNP are results from two Phase III clinical studies of brexpiprazole as adjunctive treatment to antidepressant therapy (ADT) in adults with major depressive disorder (MDD).*

Otsuka Pharmaceutical Co., Ltd. (Otsuka) and H. Lundbeck A/S (Lundbeck) today announced the presentation of Phase III study results evaluating the effects of an investigational compound, brexpiprazole, as monotherapy in adult patients with schizophrenia at the 53rd Annual Meeting of the American College of Neuropsychopharmacology (ACNP) in Phoenix, Arizona. The data were 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."

"Schizophrenia is a debilitating condition and patients often struggle to maintain a treatment regimen for multiple reasons, including lack of efficacy and undesired side effects," 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 author of one of the study reports. *"Therefore, additional treatment options are needed. The signals of efficacy, together with the favorable side effect profile observed in this study, support the use of brexpiprazole in this patient population."*

Schizophrenia Study Results

The poster, "Brexpiprazole for the Treatment of Acute Schizophrenia: A Randomized, Controlled Trial," (NCT01396421) evaluated the efficacy and tolerability of brexpiprazole in adult patients with acute schizophrenia. The pivotal Phase III trial randomized 636 patients with acute schizophrenia to fixed doses of brexpiprazole (0.25mg, 2mg or 4mg) or placebo (randomized 1:2:2:2) respectively for 6 weeks.

The results indicated:

- Brexpiprazole 4mg and 2mg demonstrated greater improvement than placebo in the primary endpoint of change from baseline to Week 6 in Positive and Negative Syndrome Scale (PANSS) Total Score (4mg: -19.65, p=0.0006 and 2mg: -20.73, p=<0.0001 vs. placebo -12.01; 0.25mg was similar to placebo -14.90).
- Key secondary endpoint results, the change in Clinical Global Impression-Severity Scale (CGI-S) score at Week 6, supported the primary results (4mg: -1.20, p=0.0012; 2mg: -1.15, p=0.0056 vs. placebo -0.82)
- Overall, approximately 65% of patients completed the 6-week study. Discontinuations due to adverse events were 13.3%, 8.2%. 9.4% and 17.4%, while discontinuations due to lack of efficacy were 7.8%, 9.3%, 3.9% and 9.8% in the brexpiprazole 0.25mg, 2mg, 4mg and placebo groups, respectively.
- 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 0.25mg, 2mg, 4mg, versus placebo groups, respectively.

The poster, "A Multicenter, Randomized, Controlled, Phase III Trial of Fixed-dose Brexpiprazole for the Treatment of Adults with Acute Schizophrenia," (NCT01393613) showcased results from a pivotal Phase III trial that randomized 674 patients with acute schizophrenia to fixed doses of brexpiprazole (1mg, 2mg, 4mg) or placebo (2:3:3:3) respectively for 6 weeks.

The results indicated:

- Brexpiprazole 4mg showed improvement over placebo in the primary endpoint of PANSS Total Score from baseline to Week 6 (-20.0 vs. -13.5, p=0.0022), while the 2mg (-16.6) and 1mg (-16.9) doses showed numeric improvement versus placebo (-13.5, p>0.05).
- Key secondary endpoint results, the change in CGI-S score versus placebo at Week 6, supported the primary results (4mg: -1.2, p=0.0015; 2mg: -1.0, p>0.05; 1mg: -0.9, p>0.05 vs. placebo: -0.8).
- Overall, approximately 68% of patients completed the 6-week study. Discontinuations due to adverse events were 9.2%, 5.9%. 7.1% and 12.0%, while

discontinuations due to lack of efficacy were 7.5%, 10.8%, 8.7% and 11.4% in the brexpiprazole 1mg, 2mg, 4mg and placebo groups, respectively.

- The most frequently reported TEAEs (greater than 5% in at least one brexpiprazole treatment arm and more frequent than placebo) were dyspepsia (5.8%, 3.8%, 3.3% vs. 3.3%), insomnia (12.5%, 13.4%, 15.2% vs. 14.7%) and agitation (8.3%, 8.6%, 7.1% vs. 7.1%) for 1mg, 2mg, and 4mg brexpiprazole treatment groups versus placebo, respectively.

"We and Lundbeck are proud to present these data results for the first time as a critical part of the clinical program supporting the safety and efficacy of brexpiprazole in adults with schizophrenia," said William Carson, MD, CEO, Otsuka Pharmaceutical Development & Commercialization, Inc. *"It is our hope that brexpiprazole will offer schizophrenia patients another treatment option to manage symptoms while living with this disease."*

"Schizophrenia is a complicated disease experienced by approximately 2.4 million adults in the U.S., and having more treatment options is critical to addressing unmet needs. We still lack a truly effective and predictable path toward treatment," said Anders Gersel Pedersen, MD, EVP and head of R&D in Lundbeck. *"While advances have been made, we believe brexpiprazole can be a strong new treatment choice for these patients."*

Otsuka and Lundbeck also presented results from two Phase III studies evaluating the effect of brexpiprazole as adjunctive treatment to antidepressant therapy (ADT) in patients with major depressive disorder (MDD) at ACNP. 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."

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-HT1A and dopamine D2 receptors, and an antagonist at 5-HT2A and noradrenaline alpha1B/2C receptors, all with similar high potency (< 1nM). A New Drug Application for brexpiprazole has been filed with the US FDA and the PDUFA date is in July 2015.

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About Lundbeck
H. Lundbeck A/S (LUN.CO, LUN DC, HLUYY) is a global pharmaceutical company specialized in brain diseases. For more than 50 years, we have been at the forefront of research within neuroscience. Our key areas of focus are alcohol dependence, Alzheimer's disease, bipolar disorder, depression/anxiety, epilepsy, Huntington's disease, Parkinson's disease, schizophrenia, stroke and symptomatic neurogenic orthostatic hypotension (NOH).

An estimated 700 million people worldwide are living with brain disease and far too many suffer due to inadequate treatment, discrimination, a reduced number of working days, early retirement and other unnecessary consequences. Every day,we strive for improved treatment and a better life for people living with brain disease – we call this Progress in Mind.

Read more at www.lundbeck.com/global/about-us/progress-in-mind.

Our approximately 6,000 employees in 57 countries are engaged in the entire value chain throughout research, development, production, marketing and sales. Our pipeline consists of several late-stage development programmes and our products are available in more 100 countries. We have research centres in China, Denmark and the United States and production facilities in China, Denmark, France and Italy. Lundbeck generated revenue of approximately DKK15.3 billion in 2013 (EUR2.1 billion; USD2.7 billion).

For additional information, we encourage you to visit our corporate site www.lundbeck.com.

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`.