September 24, 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

U.S. FDA ACCEPTS OTSUKA AND LUNDBECK'S FILING FOR REVIEW OF BREXPIPRAZOLE FOR THE TREATMENT OF SCHIZOPHRENIA AND AS ADJUNCTIVE THERAPY FOR THE TREATMENT OF MAJOR DEPRESSION

Otsuka Pharmaceutical Co., Ltd., a wholly-owned subsidiary of Otsuka Holdings Co. Ltd., and H. Lundbeck A/S today announced that the U.S. Food and Drug Administration (FDA) has determined that the New Drug Application (NDA) for brexpiprazole for monotherapy in adult patients with schizophrenia and for adjunctive treatment of major depressive disorder (MDD) in adult patients is sufficiently complete to allow for a substantive review.

＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊＊

- In the clinical program, brexpiprazole demonstrated improvement in symptoms in both schizophrenia and as adjunctive therapy in major depressive disorder (MDD)
- July 2015 is the anticipated completion timing of the FDA's review (based on PDUFA timeline)
- Brexpiprazole is a serotonin-dopamine activity modulator (SDAM) believed to possess a balanced combination of binding affinity and functional activities at multiple receptors in the brain

Tokyo, Japan and Valby, Denmark – September 24, 2014 – Otsuka Pharmaceutical Co., Ltd. (Otsuka) and H. Lundbeck A/S (Lundbeck) today announced that the U.S. Food and Drug Administration (FDA) has determined that the New Drug Application (NDA) for brexpiprazole for monotherapy in adult patients with schizophrenia and for adjunctive treatment of major depressive disorder (MDD) in adult patients is sufficiently complete to allow for a substantive review, and the NDA is considered filed as of September 9, 2014 (60 days after submission). The PDUFA date is July 11, 2015.

The NDA is supported by seven completed placebo-controlled clinical phase II or III studies in the proposed indications – three studies in schizophrenia and four studies with brexpiprazole as adjunctive therapy in MDD. The dossier included data from more than 6,000 participants of whom more than 5,000 received brexpiprazole.

"We and our collaborator Lundbeck are proud to have reached this juncture in the development of brexpiprazole," said William H. Carson, M.D., president and CEO of Otsuka Pharmaceutical Development & Commercialization, Inc. "In view of the importance of good mental health and the projected impact of mental health disorders on people affected, their families and society, future new treatment options will be indispensable."

"We are proud to have completed an extensive clinical program studying the safety and efficacy of brexpiprazole in adults with schizophrenia and those with MDD," said Anders Gersel Pedersen, EVP and head of R&D in Lundbeck. "We believe in the potential of brexpiprazole to fulfill unmet patient needs and look forward to working with the FDA throughout the NDA review."

Brexpiprazole in adult patients with schizophrenia

One clinical phase II and two clinical phase III placebo-controlled studies have been completed using brexpiprazole in adult patients suffering from schizophrenia. Across the three studies more than 1,700 patients have been randomized.

In the first pivotal phase III study randomizing approximately 625 patients, brexpiprazole 2 mg/day and 4 mg/day both demonstrated greater improvement of symptoms relative to placebo as measured by change from baseline in the Positive and Negative Syndrome Scale (PANSS) Total Score at week 6 ($p<0.05$). Results of the key secondary endpoint supported primary results.

In the second pivotal phase III study randomizing approximately 650 patients, brexpiprazole 4 mg/day again demonstrated greater improvement of symptoms relative to placebo ($p<0.05$) in change from baseline in the PANSS Total Score at Week 6. Brexpiprazole 2 mg/day showed numerical improvement ($p>0.05$) over placebo at Week 6.

The results from the clinical phase II study[i] were presented at the 24th Annual US Psychiatric and Mental Health Congress in November 2011. The study showed a clinically meaningful improvement from baseline measured by PANSS total score at week 6, although it did not achieve statistical separation from placebo.[ii]

In the placebo-controlled phase II and III studies, the rates of discontinuation due to adverse events were 8.1% for patients receiving brexpiprazole compared to 12.7% of patients receiving placebo; the only adverse event that occurred in more than 5% of brexpiprazole patients and more frequently than placebo was akathisia (5.8% vs. 4.5%).

Brexpiprazole as adjunctive therapy in major depressive disorder (MDD)

Four studies have been included in the dossier using brexpiprazole as adjunctive therapy for adult patients suffering from MDD who had demonstrated a consistent, inadequate response to at least two regimens of prior antidepressant treatment. Patients with MDD and an inadequate response to one to three antidepressants were enrolled and received antidepressants for 8 weeks, single blinded, in the two phase III studies. Patients

with an inadequate response during this prospective phase were provided antidepressant therapy and randomized adjunctive treatment with either brexpiprazole or placebo for 6 weeks. The primary efficacy endpoint was the change in MADRS (Montgomery–Åsberg Depression Rating Scale) Total Score from baseline at week 6. MADRS is a commonly used scale to assess the range of symptoms in patients with MDD. Across the four studies, more than 3,900 patients entered the prospective phase and more than 1,800 patients were included in the randomized phase of the studies.

The first pivotal phase III results were presented in a poster session at the 22nd European Psychiatry Association Congress (EPA) in March 2014.[iii] This two-arm phase III study randomized approximately 380 patients and demonstrated an improvement of symptoms with an antidepressant plus 2 mg brexpiprazole that was greater than an antidepressant plus placebo ($p<0.001$).[iv]

The second pivotal phase III study was a three-arm study in which approximately 675 patients were randomized to treatment with an antidepressant plus either placebo, 1 mg brexpiprazole or 3 mg brexpiprazole.[v] Patients in both brexpiprazole treatment groups showed greater improvement in symptoms as measured by the MADRS compared to placebo (1 mg $p>0.05$, 3 mg $p<0.05$). Results of the second pivotal phase III study in MDD have not yet been published.

The first clinical phase II[vi] study randomized approximately 425 patients in four arms and was presented at the 164th Annual Meeting of the American Psychiatric Association in May 2011. Patients exhibited greater improvements than adjunctive placebo in MADRS Total score with the 1.5 (±0.5) mg/day dose of brexpiprazole after six weeks of treatment ($p<0.05$ vs. placebo).[vii] The second phase II study in MDD randomizing approximately 372 patients has not yet been published but supports the findings in the first studies.

Across the four placebo-controlled phase II and III studies, over 90% of patients completed the studies. The rates of discontinuation due to adverse events were 2.9% for patients receiving brexpiprazole compared to 0.8% of patients receiving placebo; the only adverse events that occurred in more than 5% of brexpiprazole patients and more frequently than placebo were akathisia (8.6% vs. 2.8%) and weight increased (7.3 vs. 1.9%).

Full data from the four clinical phase III studies in the two indications will be made available through scientific disclosure at upcoming medical congresses and in scientific publications. Data from the clinical phase III program in schizophrenia and adjunctive therapy in MDD has been submitted to the 53rd Congress of American College of Neuropsychopharmacology (ACNP) on 7-11 December 2014 in Phoenix, Arizona.

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 at similar potency, and an antagonist at 5-HT_{2A} and noradrenaline $alpha_{1B/2C}$ receptors.

About Otsuka Pharmaceutical Co., Ltd.

Otsuka Pharmaceutical Co., Ltd. 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 leading firm 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 more powerfully than words how Otsuka is a "big venture" company at heart, applying a youthful spirit of creativity in everything it does.

Otsuka Pharmaceutical Co., Ltd., 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 chairman Akihiko Otsuka is the third generation of Otsuka family members to lead the business, whose origins date from 1921. The Otsuka Group has business operations in 25 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 Pharmaceutical 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.

---

[i] Clinicaltrials.gov ID: NCT00905307

[ii] McQuade, R., Hobart, M., Forbes, R.A., Pfister, S., L.B. Duncan, S. Wu, J. Ouyang, Skuban, A., Sanchez, R.: *"A Phase II trial assessing the efficacy and safety of OPC-34712 in the acute treatment of adult schizophrenia (Study 331-07-203)"*; presented at 24th Annual US Psychiatric and Mental Health Congress, 7-11 November 2011, Las Vegas, NV, USA

[iii] Thase, M.E., Hobart, M., Augustine, C., Youakim, J.M., Zhang, P., Hefting, N., et al. Efficacy and safety of adjunctive brexpiprazole (OPC-34712) in major depressive disorder (MDD): A phase III, randomized, placebo-controlled study. European Psychiatry; 29 (Supp. 1).

[iv] Clinicaltrials.gov ID: NCT01360645

[v] Clinicaltrials.gov ID: NCT01360632

[vi] Clinicaltrials.gov ID: NCT00797966

[vii] Thase, M.E., Fava, M., Hobart, M., Skuban, A., Zhang, P., McQuade, R.D., et al: *"Efficacy and Safety of Adjunctive OPC-34712 in Major Depressive Disorder: A Phase II, Randomized, Placebo-Controlled Study"*