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For Immediate Release

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OTSUKA PHARMACEUTICAL CO., LTD. ANNOUNCES RESULTS FROM A PHASE 2 STUDY OF INVESTIGATIONAL PRODUCT OPC-34712 AS ADJUNCTIVE THERAPY IN ADULTS WITH MAJOR DEPRESSIVE DISORDER

– Data from Phase 2 trial demonstrated improvement in primary efficacy endpoint for patients receiving adjunctive OPC-34712 compared to placebo and support Phase 3 development; Results presented at 164th Annual Meeting of the American Psychiatric Association –

(HONOLULU, MAY 15, 2011) – Otsuka Pharmaceutical Co., Ltd. (OPC) and Otsuka Pharmaceutical Development & Commercialization, Inc. (OPDC), both subsidiaries of Otsuka Holdings Co., Ltd., today announced results from a Phase 2 clinical trial of OPC-34712, a novel D_2 dopamine partial agonist investigational product. In a six-week, double-blind, randomized, placebo-controlled study, OPC-34712 (1.5 ± 0.5 mg), when added to antidepressant therapy (ADT) in adult patients with major depressive disorder (MDD), who had exhibited an inadequate response to ADT, demonstrated improvement in the Montgomery Åsberg Depression Rating Scale (MADRS) Total Score (p=0.0303), the primary endpoint of the study.

"These data represent proof-of-concept that OPC-34712 may be effective as adjunctive therapy in treating major depressive disorder in patients with an inadequate response to ADT," said William H. Carson, M.D., President and CEO, OPDC. "Importantly, these data allow us to advance to Phase 3 development for OPC-34712 with confidence."

Trial results were presented at the American Psychiatric Association's 2011 annual meeting. "Because many patients who suffer from major depressive disorder do not respond adequately to existing therapies, it's critical that we continue to investigate new compounds as adjunctive therapy," said Study Investigator Michael E. Thase, M.D., Professor of Psychiatry, University of Pennsylvania School of Medicine. "The findings from this study advance our knowledge about the utility of adjunctive agents in patients who do not optimally respond to antidepressants alone."

OPC-34712 is a novel investigational psychotherapeutic compound developed to provide improved efficacy and tolerability (e.g., less akathisia, restlessness and/or insomnia) over established adjunctive treatments for MDD. The compound has broad activity across multiple monoamine systems

and exhibits reduced partial agonist activity at D_2 dopamine receptors and enhanced affinity for specific serotonin receptors (e.g., $5HT_{1a}$, $5HT_{2a}$ and $5HT_7$). OPC-34712 is currently poised to enter Phase 3 testing for schizophrenia and adjunctive treatment of MDD and is in Phase 2 testing for adjunctive treatment of adult ADHD.

Study Design and Findings

This Phase 2 multicenter, double-blind, placebo-controlled study randomized 429 adult MDD patients who exhibited an inadequate response to one to three ADTs in the current episode. The study was designed to assess the efficacy and safety of OPC-34712 as an adjunctive treatment to standard ADT. The ADTs included in the study were desvenlafaxine, escitalopram, fluoxetine, paroxetine, sertraline, and venlafaxine.

The study was comprised of three phases: I) a screening phase (7–28 days) that identified patients who had not responded to prior ADT within the current depressive episode; II) a prospective 8-week, single-blind phase to assess response status to ADT; and III) a randomized phase of 6-week, double-blind assessment of adjunctive OPC-34712 compared to placebo in patients who had an inadequate response to ADT. Inadequate response to prospective ADT was defined as less than 50% decrease in Hamilton Depression Rating Score at the end of the 8-week single-blind phase. Patients were randomized to daily OPC-34712 (0.15 mg, n=62; 0.50 ± 0.25 mg, n=120; or 1.5 ± 0.5 mg, n=121) or placebo (n=126) adjunctive to ADT.

The primary efficacy endpoint was mean change in the MADRS total score from baseline to Week 6 following randomization. Primary analysis objectives were to compare the efficacy of the 0.5 mg/day dose and the 1.5 mg/day dose of OPC-34712 with placebo. Improvements in mean MADRS total score, from baseline to endpoint as compared to placebo, were observed only for subjects receiving adjunctive OPC-34712 at the 1.5 mg/day dose compared with placebo ($p=0.0303$); improvements in MADRS total score for subjects receiving the 0.5 mg/day dose were not different compared with placebo ($p>0.05$).

Overall completion rates were 82–87% and similar for all treatment groups. Discontinuations due to adverse events ranged from 0.8% to 3.2% in all treatment groups compared to 0.8% in the placebo study arm. The most common adverse events associated with OPC-34712 (all doses of OPC-34712 cumulatively greater than or equal to 5 percent vs. placebo) were upper respiratory tract infection (6.9% vs. 4.8%), akathisia (6.6% vs. 3.2%), weight gain (6.3% vs. 0.8%), and nasopharyngitis (5.0% vs. 1.6%). Mean changes in body weight from baseline to last visit were: placebo = 0.77 kg, 0.15 mg OPC-34712 = 0.91 kg ($p>0.05$), 0.5 mg OPC-34712 = 1.33 kg ($p<0.05$) and 1.5 mg OPC 34712 = 1.66 kg ($p<0.05$).

About Major Depressive Disorder

Major depressive disorder (MDD) is characterized by one or more major depressive episodes, (i.e., at least two weeks of depressed mood or loss of interest accompanied by at least four additional symptoms of depression). MDD affects approximately 14.2 million American adults in a given year, and today it is often treated with antidepressants (1); however, in many cases patients fail to respond adequately to treatment (2). Depression is one of the leading causes of disability in the U.S. In 2000, the total economic burden of treating depression in the U.S. was $83.1 billion, with workplace costs, including missed days and lack of productivity due to illness, accounting for the majority of the total

economic burden (62 percent). Other economic burdens in 2000 included $26.1 billion (31 percent) for treatment costs and $5.4 billion (7 percent) for suicide-related costs (3).

1. Kessler, RC, Berglund, P, Demler, O, et al. The Epidemiology of Major Depressive Disorder Results From the National Comorbidity Survey Replication (NCS-R). JAMA. 2003; 289: 3095-3105.
2. Rush AJ, Trievdi NJ, Wisniewski SR, et al. Acute and Longer-Term Outcomes in Depressed Outpatients Requiring One or Several Treatment Steps: A STAR*D Report. Am J Psych. 2006; 163: 1905-1917.
3. Greenberg, P. Kessler, R. et al. The Economic Burden of Depression in the United States: How Did It Change Between 1990 and 2000? J Clin Psychiatry. 2003; 64: 1465-1475.

About Otsuka Pharmaceutical Co., Ltd.

Founded in 1964, 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 consumer products for the maintenance of everyday health. Otsuka is committed to being a corporation that creates global value, adhering to high ethical standards required of a company involved in human health and life, maintaining a dynamic corporate culture, and working in harmony with local communities and the natural environment. For more information, visit www.otsuka.co.jp/en.

About Otsuka Pharmaceutical Development & Commercialization, Inc.

Otsuka Pharmaceutical Development & Commercialization, Inc. is involved in conducting all phases of clinical research and development of innovative healthcare products to address unmet medical needs. OPDC is well established in the scientific community as a globally focused organization that plays a leadership role in the research and development of Otsuka's ethical healthcare products.

The Company is dedicated to the improvement of the quality of human life and health of patients around the world with a strong commitment to research and development in the areas of cardiovascular, gastrointestinal, respiratory, renal and neuroscience systems, and to treat cancer and ophthalmic disorders. OPDC is part of the Otsuka Group companies. For more information, visit www.otsuka-us.com.

OPDC is a subsidiary of Otsuka America, Inc. (OAI), which is wholly owned by Otsuka Pharmaceutical Co., Ltd. (OPC).

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