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For Immediate Release

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Otsuka and Lundbeck initiate the regulatory process for aripiprazole (once-monthly) depot formulation in Europe

- *Aripiprazole depot formulation is the first partial dopamine agonist in development for maintenance treatment of schizophrenia as extended-release injectable suspension*
- *New data presented at the 51st Annual Meeting of the American College of Neuro-psychopharmacology (ACNP) support efficacy of aripiprazole depot formulation, thus further supporting the data package for the European filing*
- *It is estimated that that schizophrenia affects approximately 1% of the adult population in Europe and the U.S., and approximately 24 million people worldwide^{1,2}*

Otsuka Pharmaceutical Co., Ltd. (Otsuka) and H. Lundbeck A/S (Lundbeck) announced the European Medicines Agency's (EMA) acceptance of the submission of a marketing authorisation application (MAA) for the approval of aripiprazole depot formulation. The application of aripiprazole depot formulation is for the maintenance treatment of adult patients with schizophrenia.

"Our efforts to bring the aripiprazole depot formulation to market demonstrate our long-term commitment to discover, develop and champion treatments for the most challenging psychiatric diseases," said William H. Carson, M.D., President and CEO, Otsuka Pharmaceutical Development & Commercialization, Inc. *"If approved, more patients with schizophrenia will have access to the efficacy and safety profile of aripiprazole in a once-monthly formulation."*

"Long-acting therapies are moving to the forefront of treatment for psychiatric disorders, and I am very excited that we now also have submitted this product in Europe," says Executive Vice President Anders Gersel Pedersen, Head of Research & Development at Lundbeck, and continues: *"If approved, aripiprazole depot formulation will offer the clinical properties of oral aripiprazole, including its safety and efficacy profile, in a form that is suited to patients who may have difficulties consistently taking their medication."*

Aripiprazole depot formulation is the first dopamine D₂ partial agonist submitted in Europe as a once-monthly injection. If approved, it will be a new treatment option to address the need for relapse prevention in patients with schizophrenia, a chronic and debilitating disease.

Results from the first clinical trial of aripiprazole depot formulation were presented in four poster presentations at the 2012 American Psychiatric Association (APA) Annual Meeting in May 2012 and have subsequently been published in the *Journal of Clinical Psychiatry* (Kane et al J Clin Psych, 2012). In December 2012, data from the

second pivotal trial were presented at the 51st Annual Meeting at the American College of Neuropsychopharmacology (ACNP) in Hollywood, Florida.

On 11 November 2011, Otsuka and Lundbeck announced an alliance to collaborate on the development and commercialisation of up to five early and late stage compounds in development. The two companies will co-commercialise aripiprazole depot formulation in the U.S. and will collaborate on the development and commercialisation of aripiprazole depot formulation in other markets worldwide. Aripiprazole depot formulation remains under review by the U.S. Food and Drug Administration (FDA).

About schizophrenia and disease relapse

Schizophrenia is a disease characterized by a distortion in the process of thinking and of emotional responsiveness. It most commonly manifests as hallucinations, paranoid or bizarre delusions, or disorganized speech and thinking, and is accompanied by significant social or occupational dysfunction. Onset of symptoms typically occurs in young adulthood, and the condition is chronic, often requiring life-long treatment to mitigate symptoms. It has been estimated that schizophrenia affects approximately 1% of the adult population in the U.S. and Europe, and approximately 24 million people worldwide^{1,2}. In the U.S., there are approximately 2.4 million adults with schizophrenia, prevalent equally in both genders^{3,4}. While there is no cure for the disease, symptoms and risk of relapse can be managed in most patients with appropriate antipsychotic treatment. However, when the disease is not managed, patients are at increased risk of disease relapse, which can cause the re-emergence or worsening of psychotic symptoms.

Relapses can occur during the natural course of schizophrenia⁵, but the major driver of recurrent episodes is medication non-adherence^{6,7}, which may be as high as 50%. There are many reasons patients stop taking their medication and they include: poor insight about their illness, side effects from their current treatment, complicated medication regimens or lack of support from their family.

Recurrent relapses can result in function decline that may never return to pre-morbid levels^{6,8,9}. The goals of long-term therapy in schizophrenia are therefore to prevent relapse, and to reduce the severity of side effects and residual symptoms^{10,11}.

About aripiprazole depot formulation

Aripiprazole depot formulation for extended-release injectable suspension, an intramuscular (IM) depot formulation of aripiprazole, is a sterile lyophilized powder that, when reconstituted with sterile water for injection, forms an injectable suspension that can be administered monthly.

After an initial injection of aripiprazole depot formulation along with an overlapping 14-day dosing of oral antipsychotic treatment, subsequent injections of aripiprazole depot formulation provide uninterrupted medication coverage for a month. Depot formulations of antipsychotic agents provide patients with stable concentrations of active drug that remain at a therapeutic range for an extended period of time and also allow psychiatrists to know when a patient does not return for a scheduled injection^{12,13}.

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 the 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.

Otsuka Pharmaceutical Co., Ltd. is a wholly owned subsidiary of Otsuka Holdings Co., Ltd., the holding company for the Otsuka Group. The Otsuka Group has business operations in 24 countries and regions around the world, with consolidated sales of approximately EUR 10.5 billion (JPY 1.15 trillion or USD 14.0 billion) for fiscal year 2011. For more information, visit www.otsuka.co.jp/en

About Lundbeck

H. Lundbeck A/S (LUN.CO, LUN DC, HLUYY) is an international pharmaceutical company highly committed to improving the quality of life for people suffering from brain disorders. For this purpose, Lundbeck is engaged in the research, development, production, marketing and sale of pharmaceuticals across the world. The company's products are targeted at disorders such as depression and anxiety, psychotic disorders, epilepsy and Huntington's, Alzheimer's and Parkinson's diseases.

Lundbeck was founded in 1915 by Hans Lundbeck in Copenhagen, Denmark. Today Lundbeck employs approximately 6,000 people worldwide. Lundbeck is one of the world's leading pharmaceutical companies working with brain disorders. In 2011, the company's revenue was DKK 16.0 billion (approximately EUR 2.1 billion or USD 3.0 billion). For more information, please visit www.lundbeck.com.

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² World Health Organization (WHO). Schizophrenia Fact Sheet. 2010. Available at http://www.who.int/mental_health/management/schizophrenia/en/. Accessed July 16, 2012

³ Regier, Darrel et al. The de Facto US Mental and Addictive Disorder Service System. *Arch Gen Psychiatry*. 1993; 50: 85-94.

⁴ Topics-Statistics: Schizophrenia. 2010. Available at <http://wwwapps.nimh.nih.gov/health/publications/the-numbers-count-mental-disorders-in-america.shtml#RegierServiceSystem>. Accessed July 18, 2012.

⁵ Wiersma D, Wanderling J, Dragomirecka E, et al. Social disability in schizophrenia: its development and prediction over 15 years in incidence cohorts in six European centres. *Psychol Med* 2000; 30 (5): 1155–1167

⁶ Ascher-Svanum H, Zhu B, Faries D, et al. A prospective study of risk factors for nonadherence with antipsychotic medication in the treatment of schizophrenia. *J Clin Psychiatry* 2006; 67 (7): 1114–1123

⁷ Robinson D, Woerner MG, Alvir JM, et al. Predictors of relapse following response from a first episode of schizophrenia or schizoaffective disorder. *Arch Gen Psychiatry* 1999; 56 (3): 241–247

⁸ Ayuso-Gutiérrez JL, del Río Vega. Factors influencing relapse in the long-term course of schizophrenia. *Schizophr Res* 1997; 28: 199–206.

⁹ Lieberman JA, Perkins D, Belger A, et al. The early stages of schizophrenia: speculations on pathogenesis, pathophysiology, and therapeutic approaches. *Biol Psychiatry* 2001; 50 (11): 884–897.

¹⁰ Lehman AF, Lieberman JA, Dixon LB, et al; for the Work Group on Schizophrenia. Practice guideline for the treatment of patients with schizophrenia. 2nd Edition. Arlington, VA: American Psychiatric Association; 2004. © American Psychiatric Association, 2010. Accessed at <http://psychiatryonline.org/content.aspx?bookid=28§ionid=1665359#45878>. May 2012.

¹¹ Falkai P, Wobrock T, Lieberman J, et al. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for biological treatment of schizophrenia, Part 2: Long-term treatment of schizophrenia. *World J Biol Psychiatry* 2006; 7 (1): 5–40

¹² Patel MX, David AS. “Why aren't depot antipsychotics prescribed more often and what can be done about it?” *Adv Psychiatr Treat*, 2005; 11: 203-213.

¹³ Kane, JM et al. “Guidelines for depot antipsychotic treatment in schizophrenia.” *Eur Neuropsychopharmacol*, 1998; 8(1): 55-66.