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For Immediate Release

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FDA APPROVES ONCE-MONTHLY ABILIFY MAINTENA™ (ARIPIPRAZOLE) FOR EXTENDED-RELEASE INJECTABLE SUSPENSION FOR THE TREATMENT OF SCHIZOPHRENIA

Otsuka Pharmaceutical Co., Ltd., a subsidiary company of Otsuka Holdings Co., Ltd., announced that the U.S. Food and Drug Administration (FDA) has approved ABILIFY MAINTENA (aripiprazole) for extended-release injectable suspension, an intramuscular (IM) depot formulation indicated for the treatment of schizophrenia.

The consolidated business forecast of fiscal 2012 announced by Otsuka Holdings on May 11, 2012 will not be changed.

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- Approval provides patients with schizophrenia the ability to access the efficacy and safety profile of oral aripiprazole in a once-monthly formulation.
- Relapse prevention is an important consideration in the treatment of patients with schizophrenia; ABILIFY MAINTENA met the Phase 3 clinical trial primary endpoint of significantly delaying time to relapse.
- ABILIFY MAINTENA will be the first commercialized product from the global alliance between Otsuka and Lundbeck focused on developing Central Nervous System (CNS) therapies worldwide.

(Tokyo, Japan and Copenhagen, Denmark, March 1, 2013) – Otsuka Pharmaceutical Co., Ltd. (Otsuka) and H. Lundbeck A/S (Lundbeck) announced the U.S. Food and Drug Administration (FDA) has approved ABILIFY MAINTENA (aripiprazole) for extended-release injectable suspension, an intramuscular (IM) depot formulation indicated for the treatment of schizophrenia, on February 28 local time.

ABILIFY MAINTENA is the first dopamine D2 partial agonist approved as a once-monthly injection. It contributes a new treatment option to address the ongoing need for relapse prevention in patients with schizophrenia, a chronic, debilitating disease.

Efficacy was demonstrated in a 52-week, placebo-controlled, double-blind, randomized-withdrawal, Phase 3 maintenance trial of ABILIFY MAINTENA in patients with schizophrenia. The time to relapse was the primary endpoint. In the trial, ABILIFY MAINTENA (n=269 adult patients) significantly delayed time to relapse compared to placebo (n=134 adult patients; hazard ratio = 5.03, 95% CI = 3.15-8.02, $p<0.0001$)[1]. In a key secondary endpoint, the percentage of subjects experiencing relapse (i.e., meeting clinical trial criteria for exacerbation of psychotic symptoms/relapse) was also significantly lower with ABILIFY MAINTENA compared to placebo at the end of the study (10% vs. 40%, respectively; $p<0.0001$). Additional support for efficacy was derived from oral aripiprazole trials.

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. ABILIFY MAINTENA is not approved for the treatment of patients with dementia-related psychosis. ABILIFY MAINTENA is contraindicated in patients with a known hypersensitivity reaction to aripiprazole. Reactions have ranged from pruritus/urticaria to anaphylaxis (see Important Safety Information below).

ABILIFY MAINTENA will be the first commercialized product from the long-term global alliance between Otsuka and Lundbeck to develop CNS medicines worldwide. The companies expect the product will be available to patients in the U.S. beginning March 18.

“Protection from relapse of schizophrenia is important for patients, their families and the communities in which they live,” said study investigator John M. Kane, M.D., Chairman of Psychiatry, The Zucker Hillside Hospital, and Vice President, Behavioral Health Services, North Shore-LIJ Health System. “As a strong believer in long-acting therapies for schizophrenia, I think it is important for physicians to have a new and effective once-monthly treatment option that can help reduce the risk of relapse and manage symptoms in patients.”

Results from the clinical trial of ABILIFY MAINTENA were published in the *Journal of Clinical Psychiatry* and first presented in four poster presentations at the 2012 American Psychiatric Association Annual Meeting in May 2012.

The trial included adult patients who met DSM-IV-TR criteria for schizophrenia and who were being treated with at least one antipsychotic medication. Patients had at least a 3-year history of illness and a history of relapse or symptom exacerbation when not receiving antipsychotic treatment. Patients in the study received injections of ABILIFY MAINTENA or placebo once every four weeks; the first injection was accompanied by two weeks of concomitant administration of oral aripiprazole. The trial included a pre-planned interim analysis which demonstrated a significantly longer time to relapse ($p<0.001$) in patients randomized to the ABILIFY MAINTENA group compared to placebo-treated patients. The trial was subsequently terminated early by an independent data monitoring committee because maintenance of efficacy was demonstrated. The final analysis demonstrated a statistically significantly longer time to relapse in patients randomized

to the ABILIFY MAINTENA group than compared to placebo- treated patients (log-rank test $p<0.0001$).

ABILIFY MAINTENA 300-400 mg has been evaluated for safety in 1,287 adult patients in clinical trials in schizophrenia, with approximately 1,281 patient-years of exposure to ABILIFY MAINTENA. A total of 832 patients were treated with ABILIFY MAINTENA for at least 180 days (at least seven consecutive injections) and 630 patients treated with ABILIFY MAINTENA had at least one year of exposure (at least 13 consecutive injections). The safety profile of ABILIFY MAINTENA is expected to be similar to that of oral aripiprazole. In patients who tolerated and responded to treatment with oral aripiprazole and single-blind ABILIFY MAINTENA and were then randomized to receive ABILIFY MAINTENA or placebo injections under double-blind conditions, the incidence of adverse reactions was similar between the two treatment groups. The only commonly observed adverse reaction associated with the use of oral aripiprazole in patients with schizophrenia (incidence of 5% or greater and aripiprazole incidence at least twice that for placebo) was akathisia (aripiprazole 8%; placebo 4%).

"Our efforts to bring ABILIFY MAINTENA to market demonstrate our long-term commitment to discover, develop and champion treatments for the most challenging psychiatric diseases," said Taro Iwamoto, President and Representative Director, Otsuka Pharmaceutical Co., Ltd. "With this important approval, more patients with schizophrenia will have access to the efficacy and safety profile of ABILIFY in a once-monthly formulation. We are excited to bring ABILIFY MAINTENA to market as part of our historic alliance with Lundbeck. Both companies are deeply committed to supporting the comprehensive needs of the mental health community, including patients, healthcare providers, caregivers and advocates."

Commenting on the first regulatory approval from the long-term alliance established between Otsuka and Lundbeck, Ulf Wiinberg, Chief Executive Officer, Lundbeck said, "ABILIFY MAINTENA represents an important treatment option for patients and their physicians and caregivers seeking an alternative long-term maintenance treatment for schizophrenia, and we are pleased to join Otsuka in launching the first product as part of our extensive global alliance. The launch of ABILIFY MAINTENA also represents Lundbeck's first entry into the U.S. psychiatry market, expanding our central nervous system focus strategically in the U.S."

On November 11, 2011 Otsuka Pharmaceutical Co., Ltd. and H. Lundbeck A/S announced the formation of an alliance to collaborate on the development and commercialization of up to five early and late stage compounds in development. The two companies will co-commercialize ABILIFY MAINTENA in the U.S. and will collaborate on the development and commercialization of aripiprazole IM depot formulation in other markets worldwide.

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.[2,3] In the U.S., there are approximately 2.4 million adults with schizophrenia, prevalent equally in both genders.[4,5] 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.[6]

Relapse of schizophrenia can occur when a patient no longer responds to antipsychotic medication or when patients stop taking their medication. 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.

About ABILIFY MAINTENA (aripiprazole)

ABILIFY MAINTENA for extended-release injectable suspension, an 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. ABILIFY MAINTENA is indicated for the treatment of schizophrenia.

After an initial injection of ABILIFY MAINTENA along with an overlapping 14-day dosing of oral antipsychotic treatment, subsequent injections of ABILIFY MAINTENA provide uninterrupted medication coverage for 30 days at a time. Depot formulations of antipsychotic agents provide patients with concentrations of active drug that remain at a therapeutic range for an extended period of time.[7,8]

IMPORTANT SAFETY INFORMATION for ABILIFY MAINTENA™ (aripiprazole) for extended-release injectable suspension

Increased Mortality in Elderly Patients with Dementia-Related Psychosis

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk (1.6 to 1.7 times) of death compared to placebo (4.5% vs 2.6%, respectively). Analyses of 17 placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. ABILIFY MAINTENA is not approved for the treatment of patients with dementia-related psychosis.

Contraindication: Known hypersensitivity reaction to aripiprazole. Reactions have ranged from pruritus/urticaria to anaphylaxis.

Cerebrovascular Adverse Events, Including Stroke: Increased incidence of cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, have been reported in clinical trials of elderly patients with dementia-related psychosis treated with oral aripiprazole.

Neuroleptic Malignant Syndrome (NMS): A potentially fatal symptom complex sometimes referred to as NMS may occur with administration of antipsychotic drugs, including ABILIFY MAINTENA. Rare cases of NMS occurred during aripiprazole treatment. Signs and symptoms of NMS include hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (e.g., irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. The management of NMS should include: 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy; 2) intensive symptomatic treatment and medical monitoring; and 3) treatment of any concomitant serious medical problems for which specific treatments are available.

Tardive Dyskinesia (TD): The risk of developing TD, potentially irreversible, abnormal, involuntary movements, has been associated with administered antipsychotic drugs. Counsel patients to notify their physician if they notice any movements which they cannot control in their face, tongue, or other body part. The syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. There is no known treatment for established TD, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. ABILIFY MAINTENA should be prescribed in a manner that is most likely to minimize the occurrence of TD.

Metabolic Changes: Atypical antipsychotic drugs have been associated with metabolic changes that include:

- **Hyperglycemia/Diabetes Mellitus:** Hyperglycemia, in some cases extreme and associated with ketoacidosis, coma, or death, has been reported in patients treated with atypical antipsychotics including aripiprazole. Patients with diabetes should be regularly monitored for worsening of glucose control; those with risk factors for diabetes should undergo baseline and periodic fasting blood glucose testing. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia should also undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.

- **Dyslipidemia:** Undesirable alterations in lipids have been observed in patients treated with atypical antipsychotics. There were no significant differences between aripiprazole- and placebo-treated patients in the proportion with changes from normal to clinically significant

levels for fasting/nonfasting total cholesterol, fasting triglycerides, fasting low-density lipoproteins (LDLs), and fasting/nonfasting high-density lipoproteins (HDLs).

- **Weight Gain:** Weight gain has been observed. Clinical monitoring of weight is recommended.

Orthostatic Hypotension: Aripiprazole may cause orthostatic hypotension. ABILIFY MAINTENA should be used with caution in patients with known cardiovascular disease, cerebrovascular disease, or conditions which would predispose them to hypotension.

Leukopenia, Neutropenia, and Agranulocytosis: Leukopenia, neutropenia, and agranulocytosis have been reported. Patients with a history of clinically significant low white blood cell (WBC) count or drug-induced leukopenia/neutropenia should have their complete blood count monitored frequently during the first few months of therapy while receiving ABILIFY MAINTENA. In such patients, consider discontinuation of ABILIFY MAINTENA at the first sign of a clinically significant decline in WBC count in the absence of other causative factors.

Seizures/Convulsions: ABILIFY MAINTENA should be used with caution in patients with a history of seizures or with conditions that lower the seizure threshold.

Potential for Cognitive and Motor Impairment: ABILIFY MAINTENA may impair judgment, thinking, or motor skills. Instruct patients to avoid operating hazardous machinery including automobiles until they are certain ABILIFY MAINTENA does not affect them adversely.

Body Temperature Regulation: Disruption of the body's ability to reduce core body temperature has been attributed to antipsychotic agents. Advise patients regarding appropriate care in avoiding overheating and dehydration. Appropriate care is advised for patients who may exercise strenuously, may be exposed to extreme heat, receive concomitant medication with anticholinergic activity, or are subject to dehydration.

Dysphagia: Esophageal dysmotility and aspiration have been associated with ABILIFY MAINTENA; use caution in patients at risk for aspiration pneumonia.

Alcohol: Advise patients to avoid alcohol while taking ABILIFY MAINTENA.

Concomitant Medication: Dosage adjustments are recommended in patients who are CYP2D6 poor metabolizers and in patients taking concomitant CYP3A4 inhibitors or CYP2D6 inhibitors for greater than 14 days. If the CYP3A4 inhibitor or CYP2D6 inhibitor is withdrawn, the ABILIFY MAINTENA dosage may need to be increased. Avoid the concomitant use of CYP3A4 inducers with ABILIFY MAINTENA for greater than 14 days because the blood levels of aripiprazole are decreased and may be below the effective levels. Dosage adjustments are not recommended for patients with concomitant use of CYP3A4 inhibitors, CYP2D6 inhibitors or CYP3A4 inducers for less than 14 days.

Most commonly observed adverse reaction: The safety profile of ABILIFY MAINTENA is expected to be similar to that of oral aripiprazole. In patients who tolerated and responded to oral aripiprazole and single-blind ABILIFY MAINTENA and were then randomized to receive ABILIFY MAINTENA or placebo injections, the incidence of adverse reactions was similar between the two treatment groups. The adverse reaction ≥ 5% incidence and at least twice the rate of placebo for oral aripiprazole vs. placebo, respectively, was:

- Akathisia (8% vs 4%) in adult patients with schizophrenia.

Injection Site Reactions: In the open-label, stabilization phase of a study with ABILIFY MAINTENA in patients with schizophrenia, the percent of patients reporting any injection site-related adverse reaction was 6.3% for ABILIFY MAINTENA-treated patients.

Dystonia is a class effect of antipsychotic drugs. Symptoms of dystonia may occur in susceptible individuals during the first days of treatment and at low doses.

Pregnancy/Nursing: Based on animal data, may cause fetal harm. ABILIFY MAINTENA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Aripiprazole is excreted in human breast milk. A decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

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 ¥1,154.6 billion for fiscal year 2011. For more information, visit www.otsuka.co.jp/en.

About H. Lundbeck A/S

H. Lundbeck A/S (LUN.CO, LUN DC, HLUKY) 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 psychotic disorders, depression, anxiety, epilepsy, Huntington's, Alzheimer's and Parkinson's diseases.

Lundbeck's U.S. business is based in Deerfield, Illinois. To learn more about Lundbeck in the U.S., visit www.lundbeckus.com.

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 2.2 billion or USD 3.0 billion). For more information, please visit www.lundbeck.com.

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