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Corporate Release

US FDA approves the labeling update of Abilify Maintena® (aripiprazole) for extended-release injectable suspension to describe new clinical data for the treatment of acutely relapsed adults with schizophrenia

- *Labeling update provides description of controlled clinical study of Abilify Maintena for treating adult patients experiencing acute relapses of schizophrenia*
- *Approval was based on Abilify Maintena demonstrating efficacy, tolerability and safety in a 12-week study in acutely relapsed adults with schizophrenia*
- *Pivotal efficacy results were published in the November print edition of The Journal of Clinical Psychiatry*

Valby, Denmark, and Tokyo, Japan, 7 December 2014 - H. Lundbeck A/S (Lundbeck) and Otsuka Pharmaceutical Co., Ltd. (Otsuka) announced that the US Food and Drug Administration (FDA) approved the labeling update of Abilify Maintena® (aripiprazole) for extended-release injectable suspension. The approval was based on results from a controlled clinical study of acutely relapsed adults with schizophrenia. Efficacy was demonstrated in a 12-week randomized, double-blind placebo-controlled study, which showed treatment with Abilify Maintena (with concomitant oral aripiprazole for the first two weeks) significantly improved symptoms with an acceptable safety and tolerability profile in adult patients experiencing an acute relapse of schizophrenia with an acceptable safety and tolerability profile.[i] These data were published in the November print edition of *The Journal of Clinical Psychiatry.*[ii]

Abilify Maintena, an atypical antipsychotic, was first approved by the FDA in February 2013 for intra-muscular (gluteal) use for the treatment of schizophrenia. Efficacy was demonstrated in a placebo-controlled, randomized withdrawal maintenance trial in adult patients with schizophrenia, and additional support for efficacy was derived from oral aripiprazole trials.[i,iii]

"*An acute exacerbation of psychotic symptoms, also referred to as disease relapse, is a key consideration in the management of schizophrenia, and can occur when a patient no longer responds to or stops taking antipsychotic medication*," 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. "*These data – and the updated product labeling – confirm the utility of Abilify Maintena in acutely relapsed adult patients, giving physicians an option to consider for both the initial and ongoing treatment of patients with schizophrenia.*"

Clinical trials results

Efficacy of Abilify Maintena (aripiprazole) for the treatment of acutely relapsed adults with schizophrenia was demonstrated in a 12-week multicenter, randomized, double-blind, placebo-controlled trial. The primary measure used for assessing psychiatric signs and symptoms was the Positive and Negative Syndrome Scale (PANSS), a 30-item scale that measures positive and negative symptoms of schizophrenia and general psychopathology, using a rating scale of 1 (absent) to 7 (extreme); the primary endpoint was pre-specified to be measured as the change from baseline to week 10 of treatment. All patients entering the trial were inpatients who met DSM-IV-TR criteria for schizophrenia and experienced an acute psychotic episode as defined by both PANSS total score of 80 or higher, and a PANSS score greater than 4 on each of four specific psychotic symptoms (conceptual disorganization, hallucinatory behavior, suspiciousness/persecution, unusual thought content). Patients had a mean PANSS total score of 103 at study entry.[i]

A total of 339 patients received double-blind treatment with Abilify Maintena 400 mg (n=167) or placebo (n=172), with 64.3% (Abilify Maintena) and 49.4% (placebo) of patients completing 10 weeks of treatment. The primary efficacy outcome was change from baseline to 10-week endpoint in PANSS total score and demonstrated greater improvement with Abilify Maintena than with placebo (-26.8 vs. -11.7, respectively, $p<0.0001$); statistically significant improvements with Abilify Maintena were shown at all time points measured from week 1-12.[i] The key secondary efficacy outcome was change from baseline to 10-week endpoint in Clinical Global Impression Severity of Illness Scale (CGI-S) score and also showed statistically greater improvement with Abilify Maintena than with placebo (-1.4 vs. -0.6, respectively, $p<0.0001$).[i,ii]

Safety of Abilify Maintena

The overall safety and tolerability profile of Abilify Maintena in this study was generally consistent with that observed in previous double-blind phase III studies.[iv,v] The most common reason for discontinuation at week 10 was patient withdrawal of consent in the Abilify Maintena group (19% vs. 9% for placebo) and lack of efficacy in the placebo group (29% vs. 7% for Abilify Maintena). Discontinuations due to adverse events occurred in 4% of patients receiving Abilify Maintena vs. 8% of patients receiving placebo.[ii] Common adverse reactions (≥5% and with an incidence at least 2-times greater than placebo) were increased weight (16.8% vs. 7.0%), akathisia (11.4% vs. 3.5%), sedation (5.4% vs. 1.2%) and injection site pain (5.4% vs. 0.6%).[i]

About Abilify Maintena® (aripiprazole)

Abilify Maintena (aripiprazole once-monthly) is the first and only once-monthly injection of a dopamine D_2 partial agonist. It is available in the US for the treatment of schizophrenia and in a number of European countries for maintenance treatment of schizophrenia in adult patients stabilized with oral aripiprazole. In Canada it is available for the maintenance treatment of schizophrenia in stabilized adult patients and in Australia for maintenance of clinical improvement in the treatment of schizophrenia.

Abilify Maintena, an atypical antipsychotic, is an intramuscular depot formulation of aripiprazole. It 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 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. It provides a treatment option to

address two of the most important considerations in the management of schizophrenia — improving symptoms in patients with an acute relapse of their disease and reducing the risk of relapse or the re-emergence of worsening of symptoms. Depot formulations of antipsychotic agents provide patients with concentrations of active drug that remain at a therapeutic range for an extended period of time.[ii,iiv]

About schizophrenia

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 US, and approximately 24 million people worldwide.[vi,vii] In the US, there are approximately 2.4 million adults with schizophrenia, prevalent equally in both genders.[viii,ix] While there is no cure for the disease, symptoms and risk of relapse - the re-emergence or worsening of psychotic symptoms[x] - can be managed in most patients with appropriate antipsychotic treatment.

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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).

Lundbeck's shares are listed on the stock exchange in Copenhagen under the symbol "LUN". Lundbeck has a sponsored Level 1 ADR program listed in the US (OTC) under the symbol "HLUYY". For additional information, we encourage you to visit our corporate site www.lundbeck.com.

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 employees 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 Pharmaceutical welcomes you to visit its global website at https://www.otsuka.co.jp/en/.

Safe Harbor/Forward-Looking Statements

The above information contains forward-looking statements that provide our expectations or forecasts of future events such as new product introductions, product approvals and financial performance.

Such forward-looking statements are subject to risks, uncertainties and inaccurate assumptions. This may cause actual results to differ materially from expectations and it may cause any or all of our forward-looking statements here or in other publications to be wrong. Factors that may affect future results include interest rate and currency exchange rate fluctuations, delay or failure of development projects, production problems, unexpected contract breaches or terminations, government-mandated or market-driven price decreases for Lundbeck's products, introduction of competing products, Lundbeck's ability to successfully market both new and existing products, exposure to product liability and other lawsuits, changes in reimbursement rules and governmental laws and related interpretation thereof, and unexpected growth in costs and expenses.

Certain assumptions made by Lundbeck are required by Danish Securities Law for full disclosure of material corporate information. Some assumptions, including assumptions relating to sales associated with product that is prescribed for unapproved uses, are made taking into account past performances of other similar drugs for similar disease states or past performance of the same drug in other regions where the product is currently marketed. It is important to note that although physicians may, as part of their freedom to practice medicine in the US, prescribe approved drugs for any use they deem appropriate, including unapproved uses, at Lundbeck, promotion of unapproved uses is strictly prohibited.

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[i] Prescribing Information. ABILIFY MAINTENA®(aripiprazole) for extended-release injectable suspension, for intramuscular use. December 2014.

[ii] Kane J., et al. Aripiprazole Once-Monthly in the Acute Treatment of Schizophrenia: Findings From a 12-Week, Randomized, Double-Blind, Placebo-Controlled Study. Journal of Clinical Psychiatry. 2014;75 (11): 1254–1260.

[iii] Drug Approval Reports. U.S. Food and Drug Administration (FDA). 2013. Available at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Reports.MonthlyApprovalsAll. Accessed November 11, 2014.

[iv] Kane J., et al. Aripiprazole Intramuscular Depot as Maintenance Treatment in Patients With Schizophrenia: A 52-Week, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study. Journal of Clinical Psychiatry. 2012; 73: 617-624.

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[vi] Mental Health Information: Schizophrenia. National Institute of Mental Health. 2014. Available at: http://www.nimh.nih.gov/health/topics/schizophrenia/index.shtml. Accessed on November 11, 2014.

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[ix] Mental Illness Facts and Numbers. National Alliance on Mental Illness. 2013. Available at: http://www.nami.org/factsheets/mentalillness_factsheet.pdf. Accessed October 29, 2014.

[x] Almond, S., et al. Relapse in Schizophrenia: Costs, Clinical Outcomes and Quality of Life. British Journal of Psychiatry. 2004; 184: 346-351.