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FDA approves ABILIFY MAINTENA

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Singapore:Ã?Â Otsuka Pharmaceutical and H Lundbeck announced the US Food and Drug Administration (FDA) has approved ABILIFY MAINTENAÃ?Â (aripiprazole) for extended-release injectable suspension, an intramuscular (IM) depot formulation indicated for the treatment of schizophrenia.

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 percent 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 start becoming available 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 Mr John M Kane, 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 percent; placebo 4 percent).

"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 Mr Taro Iwamoto, president and representative director, Otsuka Pharmaceutical. "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, Mr 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 US"

On November 11, 2011 Otsuka Pharmaceutical 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.