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**EMBARGOED until May 23, 2007, 3:00 p.m. PST; 6:00 p.m. EST**

**INVESTIGATIONAL STUDY EVALUATES THE EFFECTIVENESS OF  
ARIPIPRAZOLE IN ADOLESCENTS WITH SCHIZOPHRENIA**

*- Findings from an Otsuka Pharmaceutical Co, Ltd. Sponsored Study Presented at the  
American Psychiatric Association Annual Meeting -*

(SAN DIEGO, MAY 23, 2007) – In a six-week study in adolescents (13-17 years old) with schizophrenia, the Otsuka Pharmaceutical Co., Ltd. and Bristol-Myers Squibb Company (NYSE: BMY) atypical antipsychotic aripiprazole demonstrated significant improvement compared to placebo on the primary efficacy endpoint, Positive and Negative Syndrome Scale (PANSS) Total Score. In the findings first presented here at the 160<sup>th</sup> annual meeting of the American Psychiatric Association, approximately 85 percent of patients completed this six-week study.<sup>1,2</sup>

“Data on the management of schizophrenia in adolescents are limited,” said Robert Findling, M.D., Director of Child and Adolescent Psychiatry, University Hospitals Case Medical Center, Cleveland, Ohio. “The findings from this study contribute important new information about schizophrenia in adolescents.”

**Study Design and Findings**

The findings are from a six-week, randomized, double-blind, placebo-controlled study that evaluated the efficacy and safety of aripiprazole in adolescents, 13-17 years-old, with a

primary diagnosis of schizophrenia. This study, sponsored by Otsuka Pharmaceutical Co., Ltd. and its U.S. subsidiary, Otsuka Pharmaceutical Development & Commercialization, Inc. (Princeton, NJ) was conducted at 101 centers in 13 countries with 302 ethnically diverse adolescents. After a minimum three-day washout period without any antipsychotic treatment, adolescents were randomly assigned to receive one of two fixed doses of aripiprazole [10 mg/day (n=100) or 30 mg/day (n=102)] or placebo (n=100). Aripiprazole was started at 2 mg/day and titrated to the target dose. The primary efficacy endpoint was the mean change from baseline to endpoint (Week Six) in the PANSS Total Score. Secondary endpoints included the PANSS positive and negative subscales and the Clinical Global Impression of Improvement (CGI-I) scale. Important safety measures included incidence of adverse events, discontinuation from study due to adverse events, and laboratory measures.

Approximately 85 percent of 302 randomized patients completed this six-week study (83 percent of aripiprazole- and 90 percent of placebo-treated patients). Both doses of aripiprazole demonstrated improvement compared to placebo (p-value less than 0.05) in the mean change from baseline in PANSS Total Score at week six (aripiprazole 10 mg: -26.7; aripiprazole 30 mg: -28.6; placebo: -21.2).

The mean change from baseline to endpoint on PANSS Positive Subscale was: -7.6 for aripiprazole 10 mg (p-value less than 0.05), -8.1 for aripiprazole 30 mg (p-value less than 0.01), and -5.6 for placebo. The mean change from baseline to endpoint on PANSS Negative Subscale was: -6.9 for aripiprazole 10 mg (p-value less than 0.05), -6.6 for aripiprazole 30 mg, and -5.4 for placebo. Improvements were observed in CGI-I [aripiprazole 10 mg: 2.7 (p-value less than 0.05); aripiprazole 30 mg: 2.5 (p-value less than 0.01); placebo: 3.1].

In this study, the overall incidence of discontinuation due to adverse events was 4.3 percent for all treatment groups (5.4 percent of aripiprazole- and 2 percent of placebo-treated patients). The most common adverse events associated with aripiprazole (greater than 5 percent and at least twice the incidence compared to placebo) were extrapyramidal disorder (aripiprazole 10 mg: 13 percent; aripiprazole 30 mg: 21.6 percent; placebo: 5 percent), somnolence (aripiprazole 10 mg: 11 percent; aripiprazole 30 mg: 21.6 percent; placebo: 6 percent), and tremor (aripiprazole 10 mg: 2 percent; aripiprazole 30 mg: 11.8 percent; placebo: 2 percent).

No significant differences were found between aripiprazole and placebo on the Abnormal Involuntary Movement Scale (AIMS) or Barnes Akathisia Rating Scale (BARS). Significant

differences between aripiprazole and placebo were observed from baseline (aripiprazole 10 mg: 0.5; aripiprazole 30 mg: 0.3; placebo: -0.3) on the Simpson-Angus Scale (SAS) which measures signs and symptoms of Parkinsonism.

In this 6-week study, the percentage of patients on aripiprazole with greater than or equal to 7 percent increase in baseline body weight was 4 percent for aripiprazole 10 mg, 5.2 percent for aripiprazole 30 mg, and 1 percent for placebo. The mean change from baseline in weight was zero for aripiprazole 10 mg group; 0.2 kg (about 0.4 lbs) for the aripiprazole 30 mg group, and -0.8 kilograms (kg), or about 1.8 lbs, for placebo group.

Average prolactin levels were decreased relative to baseline in all treatment groups (10 mg aripiprazole, -12 ng/mL; 30 mg aripiprazole, -17 ng/mL, placebo, -9 ng/mL).

### **About Aripiprazole**

Aripiprazole is indicated for the treatment of schizophrenia including maintaining stability in adults who had been symptomatically stable on other antipsychotic medications for periods of three months or longer and observed for relapse during a period of up to 26 weeks. Aripiprazole is also indicated for the treatment of acute manic and mixed episodes associated with Bipolar I Disorder, and for maintaining efficacy in adults with Bipolar I Disorder with a recent manic or mixed episode who had been stabilized and then maintained for at least six (6) weeks. Physicians who elect to use aripiprazole for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual. Aripiprazole Injection is indicated for the treatment of agitation in adults with schizophrenia or bipolar disorder, manic or mixed.

Initially approved in November 2002, over 10 million prescriptions have been written for aripiprazole in the U.S.<sup>3</sup>

Aripiprazole is available by prescription only. Aripiprazole is available in tablets, orally disintegrating tablets, oral solution, and injection for intramuscular use.

Patients should talk to their healthcare professional for more information about aripiprazole.

**IMPORTANT SAFETY INFORMATION:**

**Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk (1.6 to 1.7 times) of death compared to placebo (4.5% vs 2.6%, respectively). Aripiprazole is not approved for the treatment of patients with dementia-related psychosis (see Boxed WARNING).**

- **Neuroleptic malignant syndrome (NMS)**—As with all antipsychotic medications, a rare and potentially fatal condition known as NMS has been reported with aripiprazole. NMS can cause hyperpyrexia, muscle rigidity, diaphoresis, tachycardia, irregular pulse or blood pressure, cardiac dysrhythmia, and altered mental status. If signs and symptoms appear, immediate discontinuation is recommended
- **Tardive dyskinesia (TD)**—The risk of developing TD and the potential for it to become irreversible may increase as the duration of treatment and the total cumulative dose increase. Prescribing should be consistent with the need to minimize TD. If signs and symptoms appear, discontinuation should be considered since TD may remit, partially or completely
- **Cerebrovascular adverse events** (eg, stroke, transient ischemic attack), including fatalities, have been reported at an increased incidence in clinical trials of elderly patients with dementia-related psychosis treated with aripiprazole
- **Hyperglycemia and diabetes mellitus**—Hyperglycemia, in some cases associated with ketoacidosis, coma, or death, has been reported in patients treated with atypical antipsychotics including aripiprazole. Patients with diabetes should be monitored for worsening of glucose control; those with risk factors for diabetes should undergo baseline and periodic fasting blood glucose testing. Patients who develop symptoms of hyperglycemia should also undergo fasting blood glucose testing. There have been few reports of hyperglycemia with aripiprazole

Aripiprazole may be associated with **orthostatic hypotension** and should be used with caution in patients with known cardiovascular disease, cerebrovascular disease, or conditions which would predispose them to hypotension.

As with other antipsychotic drugs, aripiprazole should be used with caution in patients with a history of **seizures** or with conditions that lower the seizure threshold.

Like other antipsychotics, aripiprazole may have the potential to **impair judgment, thinking, or motor skills**. Patients should not drive or operate hazardous machinery until they are certain aripiprazole does not affect them adversely.

Disruption of the body's ability to **reduce core body temperature** has been attributed to antipsychotics. Appropriate care is advised for patients who may exercise strenuously, be exposed to extreme heat, receive concomitant medication with anticholinergic activity, or be subject to dehydration.

As antipsychotics have been associated with **esophageal dysmotility and aspiration**, aripiprazole should be used cautiously in patients at risk for aspiration pneumonia.

As the possibility of a **suicide** attempt is inherent in psychotic illness and bipolar disorder, close supervision of high-risk patients should accompany drug therapy. Prescriptions for aripiprazole should be written for the smallest quantity consistent with good patient management to reduce the risk of overdose.

Physicians should determine if a patient is **pregnant** or intends to become pregnant while taking aripiprazole. Patients should be advised not to breast-feed while taking aripiprazole.

Physicians should advise patients to avoid alcohol while taking aripiprazole.

Both CYP3A4 and CYP2D6 are responsible for aripiprazole metabolism. Agents that induce CYP3A4 (eg, carbamazepine) could cause an increase in aripiprazole clearance and lower blood levels. Inhibitors of CYP3A4 (eg, ketoconazole) or CYP2D6 (eg, quinidine, fluoxetine, or paroxetine) can inhibit aripiprazole elimination and cause increased blood levels.

**Commonly observed adverse events** (greater than or equal to 5% incidence and at a rate at least twice the rate of placebo for aripiprazole vs placebo, respectively):

#### **Aripiprazole Oral**

In 3-week bipolar mania trials the following were reported: akathisia (15% vs 3%), constipation (13% vs 6%), sedation (8% vs 3%), tremor (7% vs 3%), restlessness (6% vs 3%), and extrapyramidal disorder (5% vs 2%).

In 4- to 6-week schizophrenia trials the following was reported: akathisia (8% vs 4%).

A similar adverse event profile was observed in a 26-week trial in schizophrenia except for a higher incidence of tremor (aripiprazole 8% vs placebo 2%).

#### **Aripiprazole Injection**

In short-term (24 hour) trials in patients with agitation associated with schizophrenia or bipolar mania the following was reported: nausea (9% vs 3%).

### **Treatment-emergent adverse events reported with:**

#### **Aripiprazole Oral**

In short-term trials of patients with schizophrenia (up to 6 weeks) or bipolar disorder (up to 3 weeks), the following were reported at an incidence greater than or equal to 10% and greater than placebo, respectively: headache (30% vs 25%), anxiety (20% vs 17%), insomnia (19% vs 14%), nausea (16% vs 12%), vomiting (12% vs 6%), dizziness (11% vs 8%), constipation (11% vs 7%), dyspepsia (10% vs 8%), and akathisia (10% vs 4%).

**Aripiprazole Injection**

In short-term (24 hour) trials, the following were reported at an incidence greater than or equal to 5% and greater than placebo, respectively: headache (12% vs 7%), nausea (9% vs 3%), dizziness (8% vs 5%), and somnolence (7% vs 4%).

**About Otsuka Pharmaceutical Co., Ltd. and Bristol-Myers Squibb**

Otsuka Pharmaceutical Co., Ltd. and Bristol-Myers Squibb are collaborative partners in the development and commercialization of aripiprazole in the United States and major European countries.

Aripiprazole was discovered by Otsuka Pharmaceutical Co., Ltd. Founded in 1964, Otsuka Pharmaceutical Co., Ltd. is a healthcare company with the mission statement: "Otsuka - people creating new products for better health worldwide." Otsuka researches, develops, manufactures and markets innovative, original products, focusing its core businesses on pharmaceutical products for the treatment of disease and consumer products for the maintenance of everyday health. The Otsuka Pharmaceutical Group comprises 87 companies and employs approximately 27,000 people in 17 countries and regions worldwide. Otsuka and its consolidated subsidiaries earned US \$6.8 billion in consolidated annual revenues in fiscal 2005.

Bristol-Myers Squibb is a global pharmaceutical and related health care products company whose mission is to extend and enhance human life.

Visit Otsuka Pharmaceutical Co., Ltd. at: [www.otsuka-global.com](http://www.otsuka-global.com)

Visit Bristol-Myers Squibb at: [www.bms.com](http://www.bms.com)

**Forward Looking Statement**

*This press release contains "forward-looking statements" as that term is defined in the Private Securities Litigation Reform Act of 1995, regarding product development. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes and results to differ materially from current expectations. No forward-looking statement can be guaranteed. There can be no guarantee that a registrational submission will be made to the FDA based on the data described in this press release or if such registrational submission is made, that it would receive FDA approval. Forward-looking statements in this press release should be evaluated together with the many uncertainties that affect Bristol-Myers Squibb's business, particularly those identified in the cautionary factors discussion in Bristol-Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2006 and in our Quarterly Reports on Form 10-Q. Bristol-Myers Squibb undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.*

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<sup>1</sup> Robb AS, Forbes RA, Marcus RN, Carson Jr. WH. Efficacy of aripiprazole in the treatment of adolescents with schizophrenia. Poster presentation NR742 at: annual meeting of the American Psychiatric Association, San Diego, California, Wednesday, May 23, 2007, 3:00 p.m. – 5:00 p.m. PST – Poster Session 7.

<sup>2</sup> Findling RL, Nyilas M, Auby P, Mallikaarjun S, McQuade RD, Marcus RN, Carson Jr. WH. Tolerability of aripiprazole in the treatment of adolescents with schizophrenia. Poster presentation NR741 at: annual meeting of the American Psychiatric Association, San Diego, California, Wednesday, May 23, 2007, 3:00 p.m. – 5:00 p.m. PST – Poster Session 7.

<sup>3</sup> IMS Auditrac NGPS: Abilify total monthly retail prescriptions: Data accessed 11/2006.