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**SIX-MONTH STUDY EVALUATED EFFECTIVENESS OF ARIPIPRAZOLE AND
STANDARD OF CARE IN MANAGEMENT OF COMMUNITY-TREATED PATIENTS
WITH SCHIZOPHRENIA**

- Data Presented at the 159th Annual Meeting of the American Psychiatric Association -

(TORONTO, May 25, 2006) – The Bristol-Myers Squibb Company (NYSE: BMY) and Otsuka Pharmaceutical Co., Ltd. atypical antipsychotic medicine, aripiprazole, demonstrated significantly greater improvement on the Investigator’s Assessment Questionnaire (IAQ) versus standard-of-care in a six-month, randomized, open-label, multicenter trial of more than 500 adults living with schizophrenia conducted in Europe.¹ The IAQ is a validated instrument that is a combined measure of efficacy, safety and tolerability, and is composed of 10 items.² Standard-of-care included treatment with one of the following atypical antipsychotics: olanzapine, quetiapine or risperidone.

The data are from a study called STAR (Schizophrenia Trial of ARipiprazole), performed in community-based treatment settings. The findings, presented today at the 159th Annual Meeting of the American Psychiatric Association (APA), also reported the effects of aripiprazole and standard-of-care on changes in metabolic measures, including weight and blood lipids,³ and change in sexual dysfunction.⁴

Details of the STAR Trial

In the STAR Trial, 555 adults with schizophrenia whose clinical symptoms were not optimally controlled or who experienced tolerability problems with their current medication were

randomized to either aripiprazole (10-30 mg/day) or one of three standard-of-care therapies: olanzapine (5-20 mg/day), quetiapine (100-800 mg/day) or risperidone (2-8 mg/day, up to 16 mg/day). The choice of standard-of-care was based on physician discretion; the results from subjects on a standard-of-care therapy were analyzed and reported as one group.

The IAQ Total Score is the sum of 10 items: positive symptoms, negative symptoms, somnolence, weight gain, signs and symptoms of prolactin elevation, akathisia, extrapyramidal symptoms (EPS), cognition, energy and mood. A lower score correlates generally with an improvement in the combined measure of efficacy, safety and tolerability.

One presentation of the STAR data (abstract NR929¹) at APA reported that at Week 26, the mean IAQ Total Score was significantly lower for adults taking aripiprazole compared with standard-of-care: 25.7 vs. 27.7 (p-value less than 0.001), respectively. Similar results were reported for the mean change in Clinical Global Impression Improvement (CGI-I) score for aripiprazole and standard-of-care. A greater proportion of aripiprazole-treated adults were rated by the investigator as "very much improved" or "much improved" based on the CGI-I scale: 44 percent aripiprazole vs. 34 percent standard-of-care (p-value equals 0.009). Adverse events occurring in at least 5 percent of adults taking aripiprazole and a greater rate than standard-of-care were: nausea (10.6% vs. 1.1%), akathisia (8.9% vs. 2.3%), headache (13.5% vs. 7.9%), agitation (5.0% vs. 1.9%), anxiety (16.0% vs. 11.3%), insomnia (24.1% vs. 7.5%) and psychotic disorder (7.4% vs. 4.9%). Adverse events occurring in at least 5 percent of the adults taking standard-of-care and a greater rate than aripiprazole were: fatigue (6.0% vs. 3.5%), weight increase (9.4% vs. 1.1%), somnolence (11.7% vs. 3.9%) and schizophrenia (6.4% vs. 6.0%).

Another STAR-based presentation (abstract NR391³) at APA reported mean changes from baseline in levels of total cholesterol, HDL-C, LDL-C, triglycerides, glucose and weight. After 26 weeks of treatment with aripiprazole or standard-of-care, respectively, results demonstrated a mean change in total cholesterol plasma levels (-20.3 mg/dL vs. -7.7 mg/dL, p-value less than 0.001), HDL-C (+2.0 mg/dL vs. +0.4 mg/dL, p-value equals 0.028), LDL-C (-13.3 mg/dL vs. -5.8 mg/dL, p-value less than 0.001), triglycerides (-46.3 mg/dL vs. -13.0 mg/dL, p-value less than 0.001), weight (-1.3 kg vs. +2.1 kg, p-value less than 0.001) and glucose levels (+0.2 mg/dL vs. +3.3 mg/dL, p-value equals 0.146, not significant).

Results reported in abstract NR361⁴ at APA included mean change from baseline in the Arizona Sexual Experience Scale (ASEX) Total Score. The ASEX is a 5-item scale to evaluate sexual dysfunction among psychiatric patients. A lower score correlates with improvement in sexual function. At Week 26, mean change from baseline in ASEX Total Score for each treatment group was -1.44 plus or minus 0.31 for aripiprazole and -0.56 plus or minus 0.34 for standard-of-care (p-value equals 0.012).

A fourth presentation (abstract NR360⁵) at APA described the major reasons healthcare professionals decided to change their patients' treatment regimen to enter the STAR study, which included the presence of negative symptoms (71%), lack of energy (59.3%), the presence of positive symptoms (50.6%), cognitive impairment (44.7%), weight gain (39.3%), somnolence (34%), mood (34.1%), extrapyramidal symptoms (19.6%), and signs and symptoms of prolactin elevation (12.4%).

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. Since its initial approval in 2002, more than seven million prescriptions have been written in the United States.

Aripiprazole is available by prescription only. Aripiprazole tablets are available in 2 mg, 5 mg, 10 mg, 15 mg, 20 mg, and 30 mg strengths. The effective dose range is 10-30 mg/day for schizophrenia patients, and 15 or 30 mg/day for Bipolar I Disorder patients. In addition to administration as a tablet, aripiprazole is available in a 1 mg/mL nonrefrigerated oral solution.

Aripiprazole is taken once daily with or without food. It is important to talk to a healthcare provider for more information about aripiprazole.

IMPORTANT SAFETY INFORMATION for Aripiprazole:**Increased Mortality in Elderly Patients With Dementia-Related Psychosis**

Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular or infectious in nature. Aripiprazole is not approved for the treatment of patients with dementia-related psychosis (see Boxed WARNING).

Aripiprazole is contraindicated in patients with a known **hypersensitivity** to the product.

As with all antipsychotic medications, including aripiprazole, a rare condition referred to as **neuroleptic malignant syndrome** (NMS) has been reported. As with all antipsychotic medications, prescribing should be consistent with the need to minimize the risk of **tardive dyskinesia** (TD).

Cerebrovascular adverse events (e.g., 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, including a significant dose response relationship in a fixed-dose trial. Aripiprazole is not approved for the treatment of patients with dementia-related psychosis.

Hyperglycemia, including some serious cases ranging from ketoacidosis, hyperosmolar coma, or death, has been reported in patients treated with atypical antipsychotics. Patients on aripiprazole should be appropriately tested before and monitored during treatment.

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.

Patients should be advised to avoid alcohol while taking aripiprazole.

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

Commonly observed adverse events reported with aripiprazole in 3-week bipolar mania trials at a greater than or equal to 5% incidence for aripiprazole and at a rate at least twice the rate of placebo include, respectively, akathisia (15% vs. 4%), constipation (13% vs. 6%), and accidental injury (6% vs. 3%).

Treatment-emergent adverse events reported with aripiprazole in short-term trials at an incidence greater than or equal to 10% and greater than placebo, respectively, include headache (31% vs. 26%), agitation (25% vs. 24%), anxiety (20% vs. 17%), insomnia (20% vs. 15%), nausea (16% vs. 12%), dyspepsia (15% vs. 13%), somnolence (12% vs. 8%), akathisia (12% vs. 5%), lightheadedness (11% vs. 8%), vomiting (11% vs. 6%), and constipation (11% vs. 7%).

The adverse events reported in a 26-week, double-blind schizophrenia trial comparing aripiprazole and placebo were generally consistent with those reported in the short-term, placebo-controlled schizophrenia trials, except for a higher incidence of tremor: 9% for aripiprazole vs. 1% for placebo.

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

Bristol-Myers Squibb and Otsuka Pharmaceutical Co., Ltd. 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 81 companies and employs approximately 26,000 people in 16 countries and regions worldwide. Otsuka and its consolidated subsidiaries earned US \$6.2 billion in consolidated annual revenues in fiscal 2004.

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

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For more information about aripiprazole and FULL PRESCRIBING INFORMATION, including

Boxed WARNING, visit: www.bms.com

Visit Bristol-Myers Squibb at: www.bms.com

Visit Otsuka Pharmaceutical Co., Ltd. at: www.otsuka-global.com/

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