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CATIE Phase 2 Data Confirm Patients Stay on Treatment Longer Because of Symptom Improvement More So Than Tolerability

Zyprexa Was Among Most Effective Atypical Antipsychotics Studied

INDIANAPOLIS, April 1, 2006 /PRNewswire-FirstCall via COMTEX News Network/ -- Eli Lilly and Company today commented on findings of the phase 2 CATIE (Clinical Antipsychotic Trial of Intervention Effectiveness) trial and provided perspective on Zyprexa's overall results. The findings from phase 2 were published in the April issue of the American Journal of Psychiatry.

CATIE phase 2 focused on the use of atypical antipsychotics to treat chronic schizophrenia and was designed to evaluate which ones were better "rescue" treatments for patients who required a medication switch in phase 1 either because the prior medication didn't work well enough or they were not able to tolerate it. This was measured by medication discontinuation for any cause.

Results indicated that patients continue medication treatment longer when given a medication that effectively controls their psychotic symptoms, and that when patients switch medications, it is more often due to the drug's lack of efficacy rather than the patient's ability to tolerate the drug.

"Results from CATIE phase 1 and 2 challenge the notion that patients discontinue their medication mainly due to side effects," said J. Steven Lambert, M.D., associate chair for clinical programs, department of psychiatry, University of Rochester Medical Center and CATIE investigator. "These findings further demonstrate the need for doctors to fully evaluate the benefit/risk profiles of atypical antipsychotics and why individualized treatment is so important to consider when treating chronic schizophrenia."

Zyprexa(R) (olanzapine) was among the most effective atypical antipsychotics studied in the second phase of CATIE for those patients who required a medication change in Phase 1.

In the efficacy arm, clozapine performed best in terms of all-cause discontinuation, followed by Zyprexa(i). In the tolerability arm, risperidone and Zyprexa performed best in terms of all-cause discontinuation, which was contrary to the study's hypothesis that ziprasidone would be the most effective atypical because it caused little or no weight gain(ii). In addition, a secondary analysis in the tolerability arm of the study showed a statistically significant reduction in positive psychotic symptoms (such as paranoid ideas or hearing voices) for patients taking Zyprexa. Zyprexa patients also had the lowest rate of hospitalizations (11 percent) among the other atypicals studied (risperidone (15 percent), ziprasidone (16 percent), and quetiapine (20 percent)(iii)). These findings are consistent with CATIE phase 1.

While there were no statistical differences among those who discontinued treatment because of intolerability among the four atypical antipsychotics studied in this arm, there were variations in the types of adverse events reported. Zyprexa patients in phase 2 experienced greater weight gain and increases in total cholesterol and triglyceride levels versus patients using the other atypical antipsychotics studied. These results are similar to data reported in phase 1. (Information about adverse events related to increases

in blood glucose levels, lipid metabolism and weight gain is included in the Zyprexa product label.)

"Results of this landmark study confirm that efficacy matters when treating this devastating illness," said Robert Baker, M.D., medical director, U.S. neuroscience, Eli Lilly and Company. "Studies such as CATIE are important for both doctors and patients as they provide insights about why patients continue or discontinue their medication treatment. This is important because patients who stay on their treatment longer may have a lower risk of relapse as well as experience fewer hospitalizations.

"Schizophrenia is a very complex neurological disorder," he added. "For reasons we do not yet fully understand, a medication that works in one person with schizophrenia may not work in another. It's important for doctors and patients to have access to a variety of medications, and it's crucial for patients to stay on the medication that works best for them."

CATIE Background

CATIE was designed to evaluate the overall clinical effectiveness of antipsychotics in the treatment of schizophrenia, as measured by any-cause medication discontinuation, a measure that integrates both the patients' and the doctors' judgment of how well a medication works, its safety and how well the patient tolerates the treatment.

If patients were experiencing issues with efficacy or tolerability on the medication they were randomized to in phase 1, they could decide with their doctors to switch medications and enroll in phase 2. In this "rescue" phase, patients could choose to enroll in the efficacy arm or the tolerability arm. In the efficacy arm, they received clozapine or were reassigned to double-blind treatment with a different atypical antipsychotic -- olanzapine, quetiapine or risperidone. In the tolerability arm, they were randomized to receive ziprasidone or one of the same three atypical antipsychotics used in the efficacy arm. Patients were given a different atypical antipsychotic than the one they received in phase 1. Time to all-cause discontinuation was measured in each study arm.

Zyprexa(R) Background

Zyprexa(R) (olanzapine) is indicated in the United States for the short- and long-term treatment of schizophrenia, acute mixed and manic episodes of bipolar I disorder, and maintenance treatment of bipolar disorder. Since Zyprexa was introduced in 1996, it has been prescribed to more than 18 million people worldwide.

Zyprexa is not approved for the treatment of patients with dementia-related psychosis. Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared with those patients taking a placebo. In addition, compared to elderly patients with dementia-related psychosis taking a placebo, there was a significantly higher incidence of cerebrovascular adverse events in elderly patients with dementia-related psychosis treated with Zyprexa.

Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics, including Zyprexa.

Prescribing should be consistent with the need to minimize the risk of neuroleptic malignant syndrome, tardive dyskinesia, seizures and orthostatic hypotension.

The most common treatment-emergent adverse event associated with Zyprexa in placebo-controlled, short-term schizophrenia and bipolar mania trials was somnolence. Other common events were dizziness, weight gain, personality disorder (COSTART term for nonaggressive objectionable behavior), constipation, akathisia, postural hypotension, dry mouth, asthenia, dyspepsia, increased appetite and tremor.

Full prescribing information, including a boxed warning, is available at <http://www.zyprexa.com>.

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(i) McEvoy, Joseph P., Joseph P., Lieberman, Stroup, Scott T. "Effectiveness of Clozapine Versus Olanzapine, Quetiapine, and Risperidone in Patients with Chronic Schizophrenia Who Did Not Respond to Prior Atypical Antipsychotic Treatment" Am J Psychiatry 2006 163: 600-610

(ii) Stroup, Scott T., Joseph P., Lieberman, McEvoy, Joseph P. "Effectiveness of Olanzapine, Quetiapine, Risperidone, and Ziprasidone in Patients with Chronic Schizophrenia Following Discontinuation of a Previous Antipsychotic" Am J Psychiatry 2006 163: 611-622

(iii) Stroup, Scott T., Joseph P., Lieberman, McEvoy, Joseph P. "Effectiveness of Olanzapine, Quetiapine, Risperidone, and Ziprasidone in Patients with Chronic Schizophrenia Following Discontinuation of a Previous Antipsychotic" Am J Psychiatry 2006 163: 611-622

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