



NEWS RELEASE - *for immediate release*

Alexza's AZ-004 Phase IIa Trial Meets Primary Endpoint in Treating Schizophrenic Patients with Acute Agitation

**Initial Analysis Shows Statistically Significant Changes
In Agitation Levels with 10 mg AZ-004**

Palo Alto, California - March 26, 2007 - Alexza Pharmaceuticals, Inc. (Nasdaq: ALXA) today announced positive initial results from its Phase IIa clinical trial of AZ-004 (*Staccato*[®] loxapine) in schizophrenic patients with acute agitation. The 10 mg dose of AZ-004 met the primary endpoint of the clinical trial, which was a statistically-significant reduction in the measure of agitation from baseline to the 2-hour post-dose time point, compared to placebo. Alexza also announced today positive top-line results from its Phase IIb clinical trial of AZ-001 (*Staccato* prochlorperazine) in patients with migraine headache, where AZ-001 met the primary endpoint of the Phase IIb clinical trial.

"AZ-004 is a product candidate that we believe could fill an important unmet need in the acute treatment of agitation in schizophrenic patients," said Thomas B. King, President and CEO of Alexza. "AZ-004 combines drug delivery speed comparable to that of an intravenous injection, but with the simplicity, convenience and ease of administration of a simple, one-breath inhalation."

"Antipsychotic drugs used to treat acute agitation are typically administered by intramuscular injection, usually in a clinic or in an emergency department," said James V. Cassella, PhD, Senior Vice President, Research and Development of Alexza. "The ability to provide a proven drug mechanism of action, coupled with rapid pharmacokinetics and patient self-administration, makes *Staccato* loxapine a potentially important new drug candidate for treating agitation in schizophrenic patients."

Clinical Trial Design

The Phase IIa clinical trial was designed as a multi-center, randomized, double-blind, placebo-controlled study of 120 patients in an in-patient clinical setting. In the trial, two doses of AZ-004 (*Staccato* loxapine in 5 and 10 mg doses) and placebo (*Staccato* device containing no drug) were tested. The primary aim of the clinical trial was to assess the safety and efficacy of a single dose of AZ-004 in acutely treating agitation in schizophrenic patients. Assessments of a patient's agitation state were conducted at serial time points using both standard agitation scales and objective measures of patient's movement over a 4-hour period, with follow-up assessments for the next 20 hours. The change in the PANSS (Positive and Negative Symptom Scale) Excited Component (PEC) score at the 2-hour post-dose time point was the primary efficacy measure for the clinical study. All results were considered statistically significant at the $p < 0.05$ level and all analyses were made on an intent-to-treat basis. Side effects were recorded throughout the clinical trial study period.



Primary Efficacy Endpoint

The 10 mg dose of AZ-004 met the primary endpoint of the clinical trial, showing a statistically significant improvement, compared to placebo. The 5 mg dose of AZ-004 did not achieve statistical significance, compared to placebo.

PEC Scores (Mean Values)

<u>Study Arms</u>	<u>Baseline Mean</u>	<u>2-hour Post-Dose Mean</u>	<u>Significance</u>
10 mg AZ-004	17.3	8.8	p=0.0005
5 mg AZ-004	17.6	10.8	p=0.1067
Placebo	17.7	12.7	na

Note: na = not applicable

Additional Efficacy Variables

The 10 mg dose of AZ-004 also exhibited a rapid onset of effect. At 20 minutes post-dose, the 10 mg dose showed statistically significant improvement in the PEC scores, compared to placebo. The effectiveness of the 10 mg dose was sustained throughout the 24-hour study period, compared to placebo.

Using the Behavioral Activity Rating Scale (BARS), the 10 mg dose of AZ-004 showed statistically significant improvement, compared to placebo, beginning at 30 minutes. This response was sustained throughout the 24-hour study period, compared to placebo.

Clinical Global Impression-Severity (CGI-S) scale ratings to measure agitation were completed at baseline, immediately prior to AZ-004 administration. At the 2-hour post-dose time point, a Clinical Global Impression-Improvement (CGI-I) evaluation was completed for each patient. Both the 10 mg and the 5 mg doses of AZ-004 showed statistically significant improvements in the CGI-I scale, compared to placebo.

Safety Evaluations

Side effects were recorded throughout the clinical trial period. The administration of AZ-004 was generally safe and well tolerated. The most common side effects reported were taste, sedation and dizziness. These side effects were generally mild to moderate in severity, and occurred in both drug and placebo dose groups. There were three serious adverse events reported associated with the trial and all occurred at least one week post dosing. None of these serious adverse events were deemed attributable to study medication.

Device Performance

All efficacy and safety analyses were completed on an intent-to-treat basis. *Staccato* devices used in the clinical trial were returned for analysis of device performance. Preliminary analysis of the returned devices and all devices routinely analyzed during quality control and ongoing stability studies related to the clinical trial materials showed a device mechanical failure rate of less than 1%.



About Schizophrenic Patients with Acute Agitation

Acute agitation is a complication of many major psychiatric disorders, including schizophrenia, bipolar disorder and dementia, characterized by an unpleasant degree of arousal, tension and irritability, frequently leading to confusion, hyperactivity and hostility. According to the National Institute of Mental Health, schizophrenia afflicts more than three million people in the United States. Agitation is one of the most common and severe symptoms of schizophrenia. Patients may seek treatment in an emergency room, a psychiatric services setting or a private psychiatric hospital, and some do not receive treatment. Treated patients are generally given an intramuscular injection of an atypical antipsychotic drug or a sedative medication. However, intramuscular injections are invasive, can take 30 to 60 minutes to begin to work, are often disconcerting to patients, and can be dangerous to the medical personnel attempting to give the injection. Alexza believes that many schizophrenic patients can make informed decisions regarding their treatment in an acute agitative state and would prefer a noninvasive treatment. Alexza also believes there is a significant unmet medical need for a faster-acting, noninvasive treatment of acute agitation in schizophrenic patients.

About AZ-004 (*Staccato* loxapine)

AZ-004 is the combination of Alexza's proprietary *Staccato* system with loxapine, a drug belonging to the class of compounds known as antipsychotics. In a Phase I dose-escalation clinical trial in healthy subjects, AZ-004 was generally well tolerated at all doses tested and there were no serious adverse events. Across all doses, pharmacokinetic analyses revealed that peak plasma levels were generally reached within the first few minutes after dosing and AZ-004 exhibited good dose proportionality. Alexza believes the non-invasive nature and rapid pharmacokinetic properties resulting from administration via the *Staccato* system make AZ-004, if approved for marketing, a viable product candidate for treating agitation episodes in schizophrenic patients.

In December 2006, Alexza entered into a licensing transaction with Symphony Capital LLC to provide \$50 million of funding through Symphony Allegro, an affiliate of Symphony Capital, for additional clinical and nonclinical development of *Staccato* loxapine and *Staccato* alprazolam. Alexza continues to be primarily responsible for the development of these two product candidates. Alexza has an exclusive purchase option to acquire all of the equity of Symphony Allegro at certain predetermined prices, and thereby reacquire the intellectual property rights that the Company licensed to Symphony Allegro.

About Alexza Pharmaceuticals

Alexza Pharmaceuticals is an emerging pharmaceutical company focused on the development and commercialization of novel, proprietary products for the treatment of acute and intermittent conditions. The Company's technology, the *Staccato* system, vaporizes unformulated drug to form a condensation aerosol that allows rapid systemic drug delivery through deep lung inhalation. The drug is quickly absorbed through the lungs into the bloodstream, providing speed of therapeutic onset that is comparable to intravenous administration, but with greater ease, patient comfort and convenience. The Company has four product candidates in clinical development; AZ-001 (*Staccato* prochlorperazine) for the acute treatment of migraine headaches, AZ-002 (*Staccato* alprazolam) for the acute treatment of panic attacks associated with panic



disorder, AZ-004 (*Staccato* loxapine) for the treatment of acute agitation in patients with schizophrenia and AZ-003 (*Staccato* fentanyl) for the treatment of patients with acute pain.

Safe Harbor Statement

This press release includes forward-looking statements regarding the development, therapeutic potential and safety of AZ-004. Any statement describing the Company's expectations or beliefs is a forward-looking statement, as defined in the Private Securities Litigation Reform Act of 1995, and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of developing and commercializing drugs. The Company's forward-looking statements also involve assumptions that, if they prove incorrect, would cause its results to differ materially from those expressed or implied by such forward-looking statements. Earlier stage clinical trial results are not necessarily predictive of later stage clinical trial results. These and other risks concerning the Company's business are described in additional detail in the Company's Form S-1 dated March 8, 2006, and the Company's Reports filed with the Securities and Exchange Commission, including those described in the section titled "Risk Factors" under the headings "We will need substantial additional capital in the future. If additional capital is not available, we will have to delay, reduce or cease operations." and "If our product candidates do not meet safety and efficacy endpoints in clinical trials, they will not receive regulatory approval, and we will be unable to market them." Forward-looking statements contained in this announcement are made as of this date, and the Company 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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