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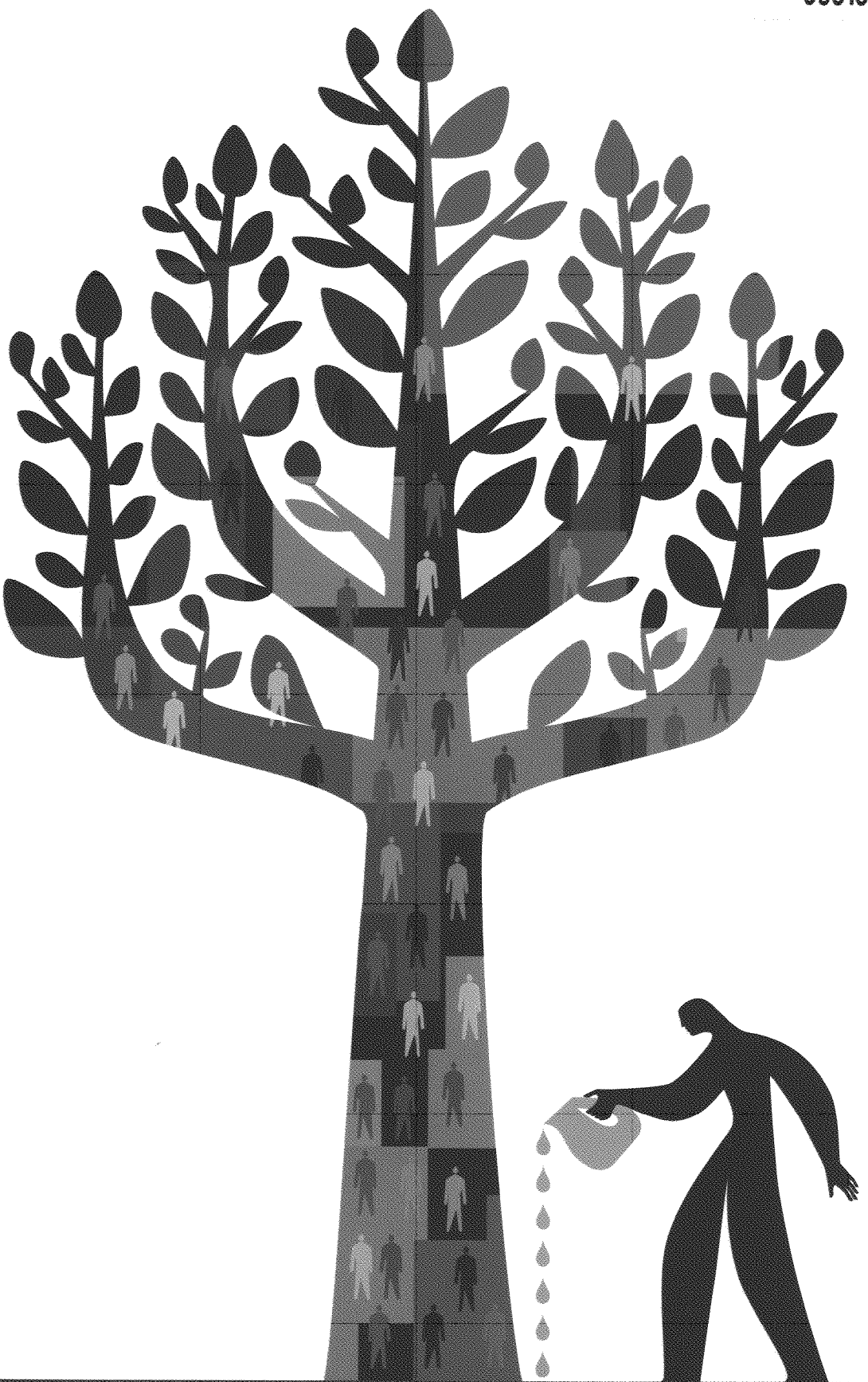
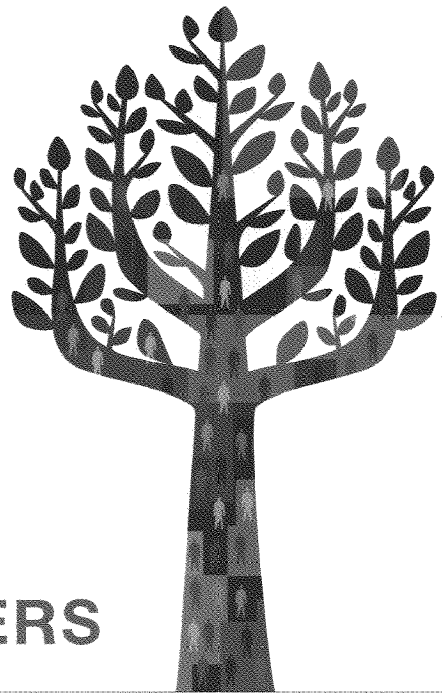
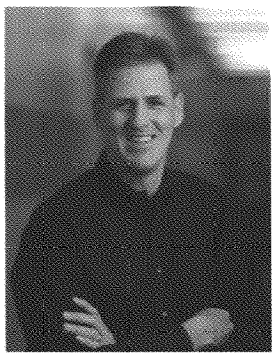


ACCELERATING RELIEF. EXPANDING MARKETS.

Alexza Pharmaceuticals 2008 Annual Report



TO OUR STOCKHOLDERS



The dual theme of this year's report — *Accelerating Relief. Expanding Markets.* — reflects the tremendous progress that Alexza has made over the past year in developing both our product pipeline and our commercial infrastructure. "Accelerating relief" refers to the compelling advantages of our Staccato® technology: an onset of therapeutic effect as fast as an intravenous injection and a non-invasive method of delivery that is as easy as breathing. We believe this combination makes *Staccato*-based drugs ideally suited to treating acute and intermittent conditions, and in 2008 that belief was strengthened by our clinical results.

OUR LEAD PRODUCT CANDIDATE AZ-004 (*STACCATO* LOXAPINE) COMPLETED TWO VERY SUCCESSFUL PHASE 3 CLINICAL TRIALS AS AN ACUTE TREATMENT OF AGITATION IN PATIENTS WITH SCHIZOPHRENIA OR BIPOLAR DISEASE. AZ-004 IS NOW ON A CLEAR PATH TOWARD AN NDA FILING, TARGETED FOR THE FIRST QUARTER OF 2010, AS A NEW ANTI-AGITATION AGENT.

The theme of "expanding markets" illustrates our belief in the significant commercial potential of our *Staccato* platform technology, in general, and AZ-004, in particular. The Phase 3 trials of AZ-004 demonstrated that our unique combination of speed, simplicity and non-invasive delivery may provide compelling advantages over current standards of care in acutely treating agitation. To stay on our aggressive timeline, we have continued to build out the in-house

WE FIRMLY BELIEVE THAT AZ-004 REPRESENTS A SIGNIFICANT IMPROVEMENT OVER TRADITIONAL METHODS OF TREATING AGITATION IN SCHIZOPHRENIC AND BIPOLAR PATIENTS, AND IT MAY HAVE THE POTENTIAL TO BECOME THE NEW STANDARD OF CARE.

manufacturing facilities and quality functions that we believe will support the commercial manufacturing of AZ-004. Importantly, we have also deepened our understanding of patient needs and how agitation is treated, and we believe that the market may be significantly larger than has been traditionally thought. Our goal now is to realize this market opportunity.

The current financial environment has greatly limited our ability to raise capital, and as a result we have taken strong steps to conserve cash. The company reduced its workforce by more than 30% in early 2009, streamlined operations, and put on hold further development of other product candidates in our pipeline. For the foreseeable future, the only way we will move a product candidate forward in the clinic is with partner funding, as we have done with AZ-004 and AZ-104 and our Symphony Capital partnership. Given near-term conditions, we are convinced this is the best strategy for Alexza's long-term success, and the company's focus for 2009 is to bring our promising lead product candidate through a successful NDA filing in early 2010.

Excellent Phase 3 Clinical Results for AZ-004

We are significantly ahead of the timeline toward this goal that I outlined in last year's letter for AZ-004. Each of the two AZ-004 Phase 3 trials we initiated, enrolled and completed in 2008 met its primary end-point, which was a statistically significant reduction in agitation from baseline levels at the two-hour post-dose time point, compared to placebo. The trial treating agitation in schizophrenics enrolled 344 patients at 24 U.S. clinical sites. The second trial, treating patients with bipolar disorder, enrolled 314 patients at 17 U.S. sites.

Both trials were in-clinic, randomized, double-blind, placebo-controlled studies that tested two dose levels, 5 mg and 10 mg. AZ-004 is a marriage of our *Staccato* system and loxapine (a well characterized anti-psychotic) specifically designed to treat agitation. Patients could receive up to three doses in a 24-hour period, though only one dose was allowed during the two hours following the initial dose.

The specific benchmark for the primary endpoint for each trial was the PANSS (Positive and Negative Symptom Scale) Excited Component score — also known as the PEC score. In both patient groups there was a statistically significant improvement in the two-hour post-dose PEC score at both the 5 mg and 10 mg dose levels.

Data also showed that AZ-004 met the trials' key secondary endpoint, which was improvement in another commonly used measurement of agitation, the Clinical Global Impression — Improvement (CGI-I) scale. With this measure, again, both the 5 mg and 10 mg doses showed highly statistically significant differences in improvement between the AZ-004 patients and those receiving placebo, as measured at the two-hour post-dose time point.

Importantly, AZ-004 also showed in both patient populations a rapid onset of effect (at 10 minutes post-dose, AZ-004 achieved statistically significant improvement in the PEC score, compared to placebo) and duration of clinical benefit (those receiving AZ-004 generally sustained their reduction in agitation for the entire 24-hour study period, compared to placebo).

We are very encouraged with this strong clinical validation of AZ-004 as a potential acute treatment for agitation in schizophrenic and bipolar patients. And we are just as excited by what we believe is confirmation of the unique competitive advantages of our *Staccato* technology.

Patients in the studies received very fast relief with our inhaled aerosolized drug, and both patients and clinicians embraced AZ-004 as an easy-to-use, less-invasive way to take a medication in an acute situation. Each of the Phase 3 trials enrolled very rapidly and the studies were completed extremely quickly — which we believe is another indication of how enthusiastically these patients, nurses and clinicians responded to the possible utility of our first *Staccato* product. We firmly believe that AZ-004 represents a significant improvement over traditional methods of treating agitation in schizophrenic and bipolar patients; if approved, it may well have the potential to fundamentally change current treatment paradigms and become a new standard of care for this patient population.

***Staccato*-Based Pipeline with Excellent Long-Term Potential**

We think that all of the *Staccato*-based product candidates in our pipeline — with their combination of speed of onset, non-invasive delivery, and ease-of-use — can provide unique advantages over existing therapies for a variety of acute and intermittent conditions, including migraine, sleeplessness, and breakthrough pain. While

we have put most of these development projects on hold in the current capital-raising environment until we establish partners or arrange other financing to bring the product candidates forward in the clinic, we have recently initiated a Phase 2b clinical trial for AZ-104 (*Staccato* loxapine) as part of our product development partnership with Symphony Capital.

AZ-104 is a lower dose version of loxapine that showed promising efficacy in a placebo-controlled, in-clinic Phase 2a trial that treated 160 migraine patients. The Phase 2b outpatient trial is expected to enroll approximately 360 patients who have migraine, with or without aura. Two doses of AZ-104 will be evaluated, as compared to placebo, and the primary efficacy endpoint is pain relief at two hours post dose using the four-point rating scale of the International Headache Society.

Also of note in our product pipeline was our mutual decision with Endo Pharmaceuticals in January 2009 to terminate our development agreement for AZ-003 (*Staccato* fentanyl). It is unfortunate that the Endo partnership has ended, but we believe AZ-003 is a promising product — the first application of our multi-dose *Staccato* device and one that targets a large, underserved market for acute breakthrough pain — and we will continue investigating possible development partners for AZ-003 and our other *Staccato*-based products that have made such solid progress in the clinic.

Preparing for Alexza's First Commercial Launch

Until we find partners to fund further development, we will not be investing in the continued clinical activity of our other product candidates. Our management focus and application of corporate resources will be primarily focused on driving AZ-004 towards what we plan to be a successful regulatory filing and, ultimately, an NDA approval.

In 2009, we will be completing four non-pivotal clinical trials for AZ-004, all in healthy normal subjects: a QT study (an analysis of heart rhythm/function while taking the drug) and three additional studies to analyze relative pharmacokinetics in smokers vs. non-smokers, to determine safety in patients with healthy lungs vs. those with asthma or pulmonary disease, and to gauge any impacts from single-day, repeat dosing on pulmonary function. We are also compiling the other clinical, nonclinical, manufacturing, and quality data for the AZ-004 NDA. We plan to file the NDA in the first quarter of 2010.

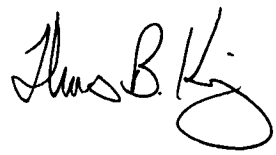
Our product launch strategy for AZ-004 has evolved from a year ago, based on significantly increased knowledge about the acute agitation market opportunity. We will still manage sourcing of components for the finished devices — supply relationships for the critical components are already in place — and will control final manufacturing and all quality aspects of the finished drug at our cGMP facility in Mountain View, California.

However, we no longer plan to build an internal sales force for the launch of AZ-004. Our in-depth market research has indicated that the size of the agitation market may be significantly larger and the physician population is more diverse than had been previously thought. Conventional wisdom has held that agitation occurs irregularly and presents almost exclusively in emergency departments. We now believe that schizophrenic and bipolar patients average upwards of ten agitation episodes a year, varying in severity from the mild to the severe end of the agitation spectrum. We also know that physicians and caregivers can and will treat agitation in a variety of settings, from emergency rooms to psychiatric care residences, outpatient clinics, and doctors' offices to prevent early-stage agitation from spiraling into a more severe episode.

In the United States, alone, schizophrenia afflicts approximately 2.4 million adults and bipolar disorder affects more than 5.7 million adults. Given our new understanding of the frequency and dynamics of agitation, we now feel that to successfully serve this potentially large group of patients and prescribing physicians, Alexza needs a well-established pharmaceutical partner with a strong presence in the psychiatric market, and we are now seeking a potential partner for AZ-004.

Clearly, the last year has been incredibly challenging for all public companies, but especially for growth companies in capital-intensive industries such as drug development. That said, we are not discouraged. We believe the capital markets will recover and we will resume development of our promising pipeline of *Staccato*-based product candidates.

In the near term, we remain focused on completing and filing our AZ-004 NDA and securing a strong marketing partnership for this promising new potential treatment for agitation. In closing, we want to express our thanks to all of our stockholders, employees and partners for their support. The company has performed well in a difficult environment. We intend to build on our foundation of success and sustain the momentum of our lead program, and we look forward to reporting on our progress in the year ahead.



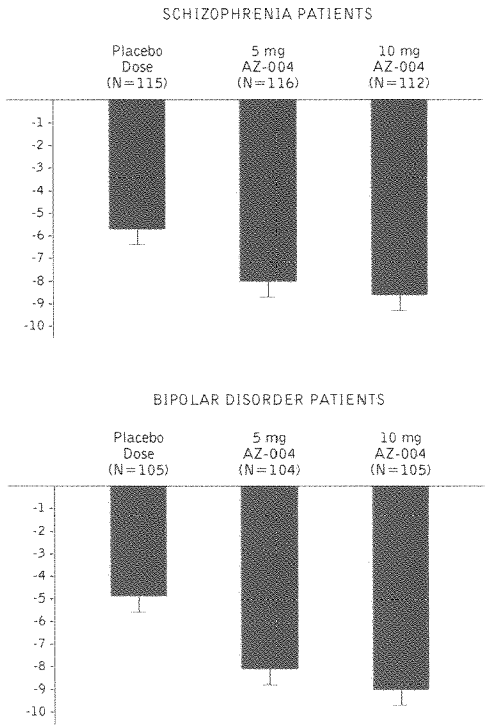
Thomas B. King
President and Chief Executive Officer
March 2009

AZ-004

EXCELLENT RESULTS IN TWO PHASE 3 CLINICAL TRIALS

LEAD PRODUCT CANDIDATE MEETS PRIMARY AND SECONDARY ENDPOINTS; UNIQUE THERAPEUTIC ADVANTAGES FOR TREATING AGITATION IN SCHIZOPHRENIC AND BIPOLAR PATIENTS.

AZ-004 Phase 3 Trial Results
Reduction in Agitation
(Change in PEC Score at 2 Hours)



Treating more than 650 patients in two pivotal trials, AZ-004 produced a statistically significant reduction in agitation in both patient populations.

Alexza's lead drug candidate AZ-004 (*Staccato* loxapine) produced very positive results during 2008 in two Phase 3 clinical trials treating agitation in schizophrenics and individuals with bipolar disorder. The first study enrolled 344 schizophrenia patients at 24 sites in the United States. The second trial enrolled 314 bipolar patients at 17 clinical sites.

Both trials were in-clinic, randomized, double-blind, and placebo controlled. Both tested AZ-004 at 5 mg and 10 mg dose levels. And both trials achieved the primary and secondary endpoints for therapeutic efficacy.

AZ-004 provided a highly statistically significant improvement in the primary endpoint of both trials: the reduction in agitation (using the PEC score) from baseline at the two-hour post-dose time point. The PEC score is a commonly used measure of a patient's level of agitation in the clinical study setting and is the endpoint used for other approved products in this indication.

AZ-004 also achieved the key secondary endpoint with a statistically significant improvement in the Clinical Global Impression — Improvement (CGI-I) score measured at two hours after dosing in both trials. The CGI-I score is important, representing a clinician's medical perspective of a patient's level of agitation and the improvement resulting from a therapy.

Other key efficacy endpoints were met in both studies, as well, including speed of onset (reduction of agitation occurred as quickly as ten minutes post-dose) and duration of effect (those using AZ-004 generally had sustained relief throughout the 24-hour study period).

UNDERSERVED PATIENT POPULATION; LARGE POTENTIAL MARKET

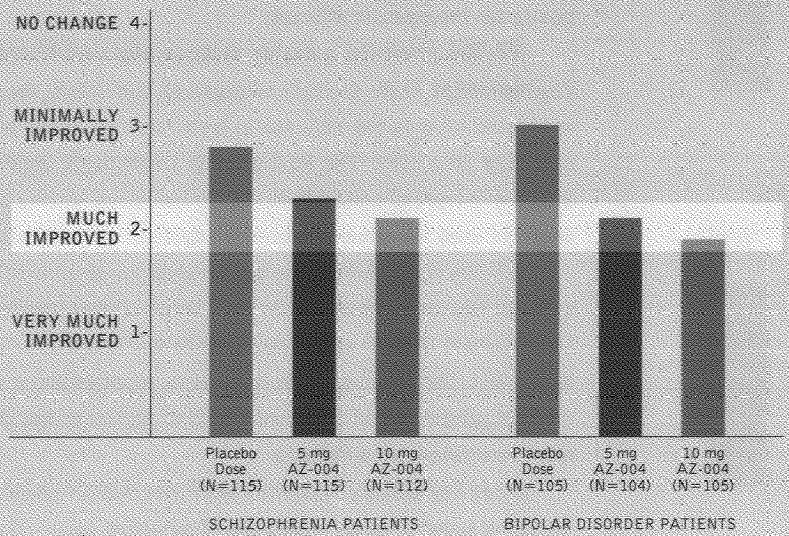
Approximately 2.4 million and 5.7 million U.S. adults suffer from schizophrenia and bipolar disorder, respectively. More than 90% of these individuals experience agitation related to their disease during their lifetime. Agitation generally manifests as an escalating series of symptoms. Patients initially feel uncomfortable, tense and restless, and as the agitation intensifies, their behavior becomes more noticeable to others as they become threatening and violent, especially if the agitation is not treated. While patients seek treatment at different points along this agitation continuum, it is the individuals exhibiting the most severe symptoms who generally require treatment with injectable drugs in emergency clinical settings that currently define the acute agitation market.

Alexza's market research indicates that this patient population is underserved and that schizophrenic and bipolar patients experiencing agitation may be more effectively treated with earlier and proactively rapid intervention. We estimate approximately 50% of treated cases today are in emergency room settings, with another 35% in in-patient setting, such as long-term care facilities. Importantly, we believe that 15% of agitation episodes are treated in a physician's office or other non-hospital environments.

Our research also indicates that the frequency of acute agitation is higher than has been traditionally understood, and that bipolar and schizophrenic patients average more than ten episodes each year. We believe that AZ-004 — with its rapid therapeutic effect and needle-free, easy-to-deliver formulation — is ideally suited to be the treatment of choice not only for emergency situations, but also for patients seeking accelerated relief in the other settings where agitation is acutely treated.

AZ-004 Phase 3 Trial Results

Clinical Global Impression-Improvement (CGI-I) Scores



As described in our data, clinicians rated the reduction in agitation produced by both doses of AZ-004, in both patient populations, as statistically significant improvements, as compared to placebo.

UNIQUELY SUITED TO TREAT ACUTE AND INTERMITTENT CONDITIONS

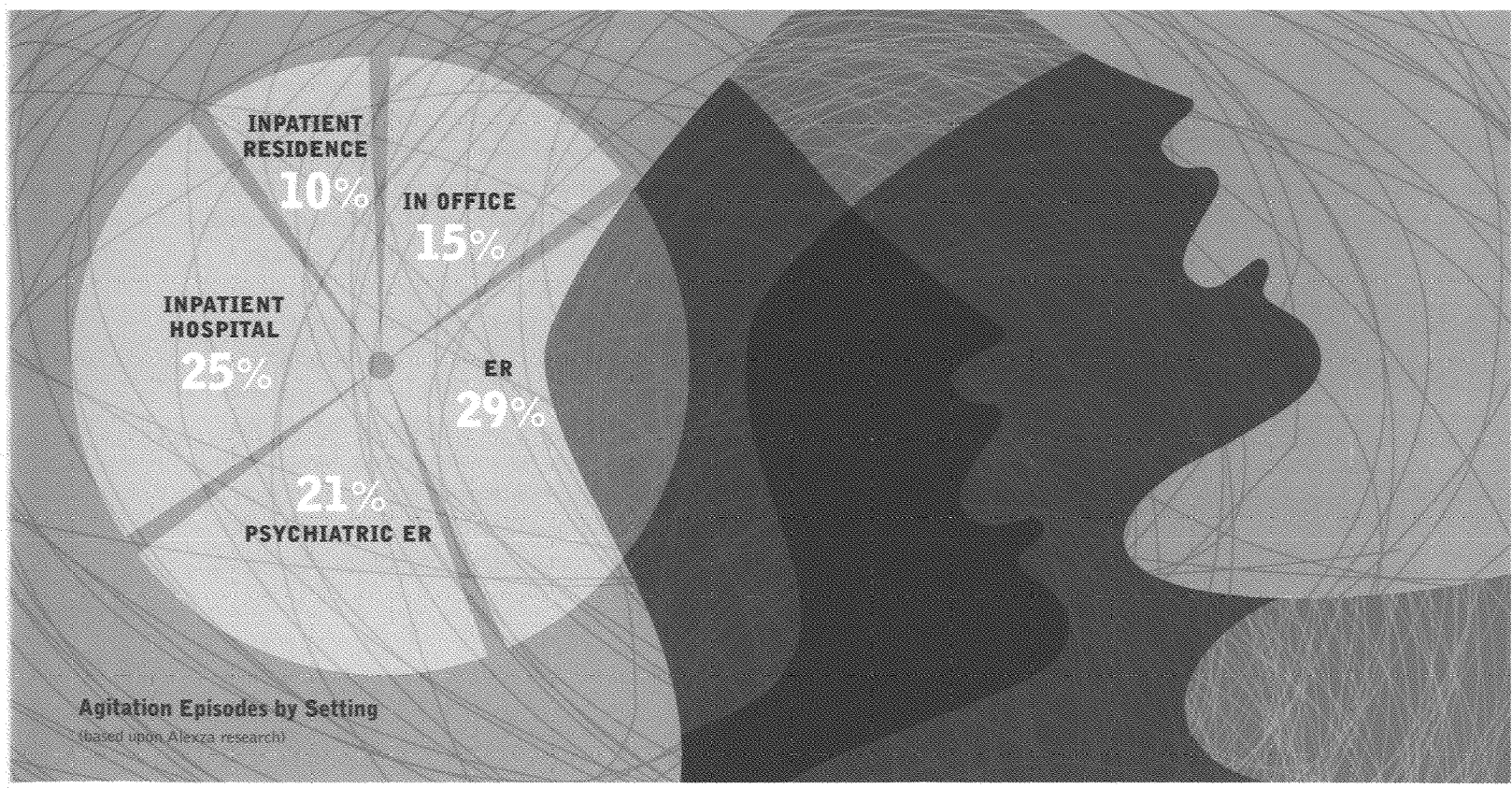
The *Staccato* system's combination of speed, simplicity, and drug-delivery consistency offers what we believe to be a new standard of care for many underserved medical markets. The American Association of Emergency Psychiatrists' Expert Consensus Guidelines for the Treatment of Behavioral Emergencies (2002) specifies three key treatment attributes for acute agitation:

- speed of onset
- reliability of medication delivery
- patient preference.

None of the current treatment options currently meets this standard — oral antipsychotics are simple and non-invasive, but slow to provide relief and can provide an inconsistent reliability of medication delivery. Intramuscular injections can provide a faster speed of onset, but are painful and often frightening to highly agitated patients.

Only AZ-004 offers all of the attributes cited in the guidelines. Built on Alexza's *Staccato* platform technology, AZ-004 delivers a precise dose of aerosolized loxapine molecules, perfectly sized to reach the tissues of the deep lung. Speed of uptake in the bloodstream mimics intravenous delivery, resulting in an onset of clinical effect that is very rapid. And taking AZ-004 is as easy and intuitive as breathing. No patients in our clinical trials have been unable to use the device.

With *Staccato*-based drugs, patients gain control of their treatment regimen, and clinicians know that dosing is consistent and accurate. Based on positive clinical results from the more than 800 subjects in all of our AZ-004 clinical trials, we believe that our *Staccato* technology has the potential to create a new standard of care not only for agitation, but for many currently underserved acute and intermittent conditions.



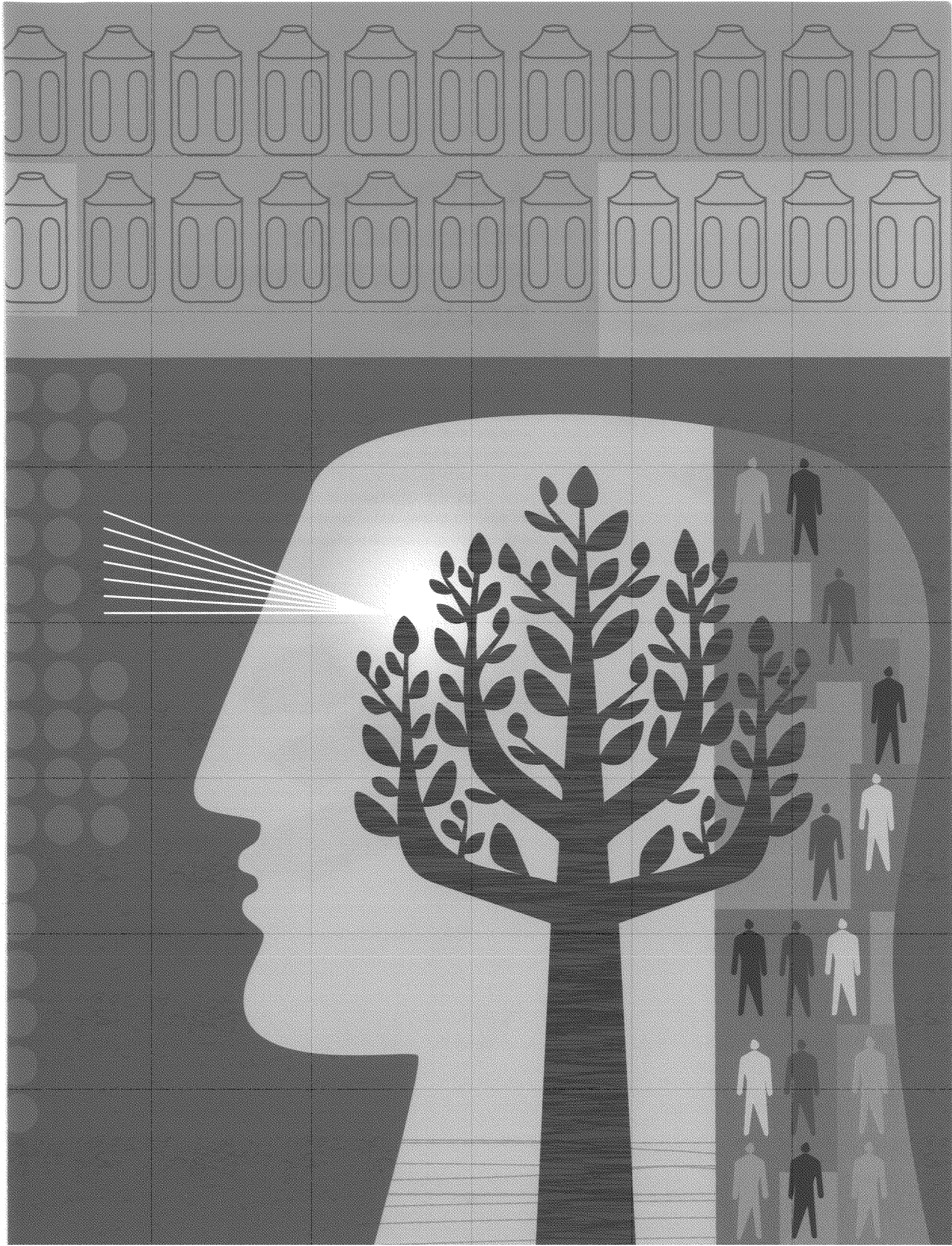
A VALUE-ADDED COMMERCIALIZATION STRATEGY

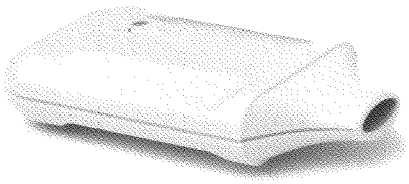
A STRONG MANUFACTURING, QUALITY, AND REGULATORY INFRASTRUCTURE DESIGNED TO ENSURE PROFITABLE COMMERCIALIZATION OF *STACCATO*-BASED PRODUCTS.

Over the past year Alexza has conducted in-depth market research on how acute agitation is treated and managed. We have concluded that the market appears to be larger and more complex than was traditionally thought. As a result, we have changed our launch strategy for AZ-004 from building an in-house sales force to seeking a pharmaceutical partner with a broad-based, well established presence in the psychiatric market.

Going forward, we expect this strategy will form the basis of our approach to the market launch of any other approved *Staccato*-based products. Those drugs that target large and more dispersed physician populations will require that we have strong commercial partners. For products that target disease indications with a smaller and more manageable universe of prescribing physicians, we will consider keeping the sales and marketing function at Alexza.

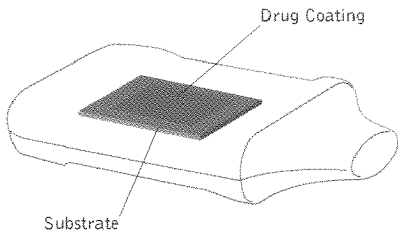
For all of our product candidates, however, we intend to maintain control of regulatory, manufacturing, and quality processes. Our cGMP manufacturing facility is designed to be able to provide the capacity to launch AZ-004. We have already put in place key technology and materials supply relationships for our *Staccato*-based products. We also have an experienced team to oversee our regulatory and commercial manufacturing activities as we move steadily closer to the expected approval and launch of Alexza's first product.

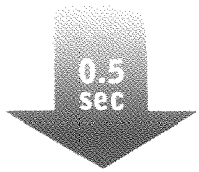




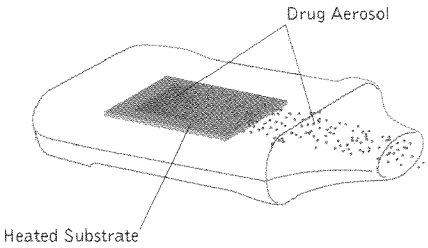
A STRONG PIPELINE OF *STACCATO*-BASED DRUGS

BEFORE INHALATION

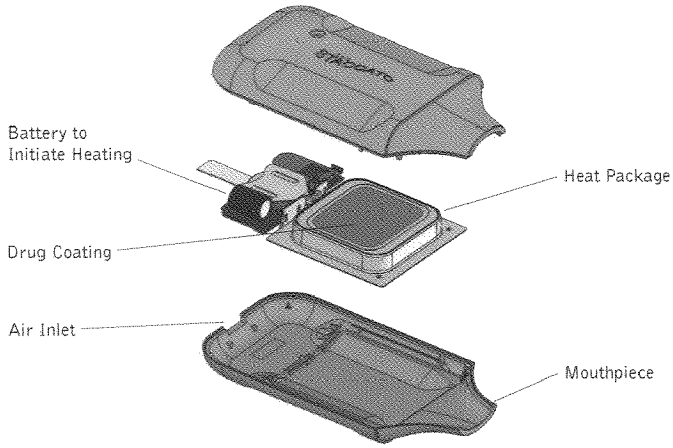


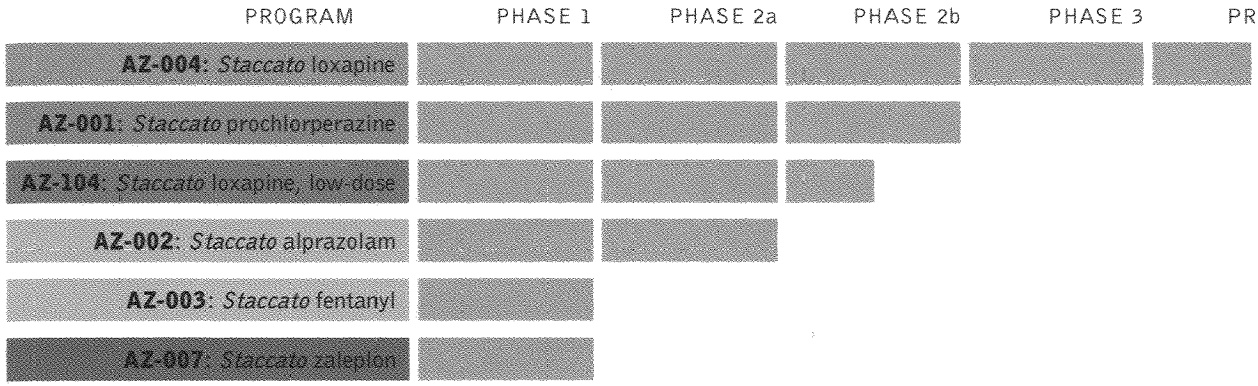


DURING INHALATION



The *Staccato* system single-dose device is comprised of a small case housing a proprietary heat package with a stainless steel substrate. A thin film of pure drug is coated onto the substrate and when a patient draws a single breath through the device, the substrate surface instantaneously heats to create a condensation aerosol of perfectly sized particles of pure drug. These molecules are drawn easily down to the narrower, more vascularized tissue of the deep lung, ensuring a highly consistent dose and rapid uptake in the bloodstream.





AZ-004 (*Staccato* loxapine)	Acute Agitation associated with Schizophrenia or Bipolar Disorder	2.4 million schizophrenia patients and 5.7 million bipolar disorder patients in the United States; agitation is a common and severe symptom.	Successfully completed two Phase 3 trials, both of which met primary and secondary endpoints. Now completing follow-on safety studies and preparing to file an NDA in the first quarter of 2010.
AZ-001 (*Staccato* prochlorperazine)	Migraine Headache	13 million people in the United States receive medication for migraine, 29.5 million people in the United States have migraine headaches*.	Phase 2 trial, human QT trial, animal toxicology study, and end-of-Phase 2 meeting with FDA completed.
AZ-104 (*Staccato* loxapine)	Migraine Headache	13 million people in the United States receive medication for migraine, 29.5 million people in the United States have migraine headaches†.	Phase 2b trial ongoing.
AZ-003 (*Staccato* fentanyl)	Breakthrough Pain	More than 25 million postoperative patients experience inadequate pain relief, despite receiving some form of pain management, and approximately 65% of patients diagnosed with cancer pain experience breakthrough pain.	Phase 1 trial (using multi-dose *Staccato* system) completed.
AZ-002 (*Staccato* alprazolam)	Panic-related Disorders		Completed proof-of-concept Phase 2a trial that did not meet primary endpoints for treating acute panic, but which did demonstrate a strong pharmacokinetic profile for delivering alprazolam.
AZ-007 (*Staccato* zaleplon)	Sleeplessness	An estimated 10-20% of people in the United States experience either chronic or occasional insomnia.	Phase 1 completed.

* Prochlorperazine is a non-triptan with potential to serve the 50% of migraine sufferers who either get little relief from or do not receive triptans because of the potential cardiovascular side-effects of triptans.

† Loxapine is a non-triptan with potential to serve the 50% of migraine sufferers who either get little relief from or do not receive triptans because of the potential cardiovascular side-effects of triptans.

CORPORATE INFORMATION

MANAGEMENT TEAM

Thomas B. King
President and Chief Executive Officer

James V. Cassella, PhD
Senior Vice President,
Research and Development

August J. Moretti
Senior Vice President and
Chief Financial Officer

Michael J. Simms
Senior Vice President,
Operations and Manufacturing

Joseph L. Baker
Vice President,
Commercial Manufacturing

Anthony Clarke, PhD
Vice President,
International Development Operations

Robert S. Fishman, MD, FCCP
Vice President,
Clinical Development

Emily Lee Kelley
Vice President,
Human Resources

Christopher Kurtz
Vice President,
Global Supply Chain and
Sustainment Engineering

Peter D. Noymer, PhD
Vice President,
Product Research and Development

Carlos A. Parra
Vice President,
Quality

Jeffrey S. Williams
Vice President,
Technology Outlicensing

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Thomas B. King
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General Partner
Delphi Ventures

J. Leighton Read, MD
General Partner
Alloy Ventures

Gordon Ringold, PhD
Chairman and Chief Executive Officer
Alavita, Inc.

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www.bnymellon.com/shareowner

INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Ernst & Young
Palo Alto, CA

STOCKHOLDER INQUIRIES

To request information from the company, including its annual report on Form 10-K, which is filed with the Securities and Exchange Commission, visit www.alexza.com or write to:

Investor Relations
Alexza Pharmaceuticals, Inc.
2091 Stierlin Court
Mountain View, CA 94043

ANNUAL MEETING

The annual meeting of stockholders will be held on Thursday, May 7, 2009 at 1:30 pm local time at Alexza Pharmaceuticals, Inc. 2023 Stierlin Court, Mountain View, CA.

STOCK INFORMATION

Alexza common stock is traded on the Nasdaq Stock Market under the symbol ALXA. As of February 28, 2009 there were 32,973,951 shares outstanding.

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

Form 10-K

For Annual and Transition Reports Pursuant to
Section 13 or 15(d) of the Securities Exchange Act of 1934

☑ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2008

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission File Number: 000-51820

SEC
Mail Processing
Section

MAR 26 2009

Washington, DC
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Alexza Pharmaceuticals, Inc.

(Exact name of Registrant as specified in its charter)

Delaware	**77-0567768**
(State or Other Jurisdiction of Incorporation or Organization)	*(I.R.S. Employer Identification Number)*

2091 Stierlin Court
Mountain View, California 94043
(Address of Principal Executive Offices including Zip Code)

Registrant's telephone number, including area code:
(650) 944-7000

Securities registered pursuant to Section 12 (b) of the Act:

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, par value $0.0001 per share	Nasdaq Global Market

Securities registered pursuant to Section 12 (g) of the Act:
None

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☑

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☑

Indicate by check mark whether the Registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☑ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of Form 10-K or any amendments to this Form 10-K. ☑

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ☐ Accelerated filer ☑ Non-accelerated filer ☐ Smaller reporting company ☐
(Do not check if a smaller reporting company)

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☑

The aggregate market value of the voting and non-voting stock held by non-affiliates of the Registrant was $98,980,416 based on the closing sale price of the Registrant's common stock on The NASDAQ Global Market on June 30, 2008. Shares of the Registrant's common stock beneficially owned by each executive officer and director of the Registrant and by each person known by the Registrant to beneficially own 10% or more of its outstanding common stock have been excluded, in that such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes. The number of outstanding shares of the Registrant's common stock as of February 28, 2009 was 32,973,951.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement for the 2009 Annual Meeting of Stockholders to be filed within 120 days after the end of the Registrant's fiscal year ended December 31, 2008 are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated therein.

ANNUAL REPORT ON FORM 10-K
FOR THE FISCAL YEAR ENDED DECEMBER 31, 2008

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The names "Alexza" and *"Staccato"* are trademarks of Alexza Pharmaceuticals, Inc. We have registered the trademarks "Alexza Pharmaceuticals," "Alexza" and "*Staccato*" with the U.S. Patent and Trademark Office. All other trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners.

PART I.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Some of the statements under "Business," "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this Annual Report constitute forward-looking statements. In some cases, you can identify forward-looking statements by the following words: "may," "will," "could," "would," "should," "expect," "intend," "plan," "anticipate," "believe," "estimate," "predict," "project," "potential," "continue," "ongoing" or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. Examples of these statements include, but are not limited to, statements regarding the following: the prospects of us receiving approval to market AZ-004, our anticipated timing for filing or receiving approval for our New Drug Application for AZ-004, the implications of interim or final results of our clinical trials, the progress and timing of our research programs, including clinical testing, our anticipated timing for filing additional Investigational New Drug Applications with the United States Food and Drug Administration, the initiation or completion of Phase 1, Phase 2 or Phase 3 clinical testing for our product candidates, the extent to which our issued and pending patents may protect our products and technology, the potential of such product candidates to lead to the development of safe or effective therapies, our ability to enter into collaborations, our future operating expenses, our future losses, our future expenditures, and the sufficiency of our cash resources. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. While we believe that we have a reasonable basis for each forward-looking statement contained in this Annual Report, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain.

In addition, you should refer to the "Risk Factors" section of this Annual Report for a discussion of other important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Annual Report will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all.

We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise. You are advised, however, to consult any further disclosures we make on related subjects in our Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and our website.

Item 1. *Business*

We are a pharmaceutical development company focused on the research, development, and commercialization of novel proprietary products for the acute treatment of central nervous system, or CNS, conditions. All of our product candidates are based on our proprietary technology, the *Staccato* system. The *Staccato* system, vaporizes an excipient-free drug to form a condensation aerosol that, when inhaled, allows for rapid systemic drug delivery. Because of the particle size of the aerosol, the drug is quickly absorbed through the deep lung into the bloodstream, providing speed of therapeutic onset that is comparable to intravenous, or IV, administration but with greater ease, patient comfort and convenience. We currently have six product candidates in various stages of clinical development, ranging from Phase 1 through late-stage Phase 3. In 2009, our focus will be on the continued rapid development of AZ-004.

We have identified approximately 200 drug compounds that have demonstrated initial vaporization feasibility for delivery with our technology. We believe that a number of these drug compounds, when delivered by the *Staccato* system, will have a desirable therapeutic profile for the treatment of acute and intermittent conditions. We are initially focusing on developing proprietary products by combining our *Staccato* system with small molecule drugs that have been in use for many years and are well characterized to create aerosolized forms of these drugs. We believe that we will be able to reduce the development time and risks associated with our product candidates, compared to the development of new chemical entities.

Our clinical-stage product candidates are:

- *AZ-004 (Staccato* loxapine*).* We are developing AZ-004 for the acute treatment of agitation in patients with schizophrenia or bipolar disorder. We project a new drug application, or NDA, submission in the first quarter of 2010.

  In December 2008, we announced positive results from the second of our two Phase 3 clinical trials of AZ-004. This trial enrolled 314 acutely-agitated patients with bipolar I disorder at 17 U.S. clinical centers. The trial was designed as an in-clinic, multi-center, randomized, double-blind, placebo-controlled study, and tested AZ-004 at two dose levels, 5 mg and 10 mg. Patients were eligible to receive up to 3 doses of study drug in a 24-hour period, depending on their clinical status. Only one dose of study drug was allowed during the first 2 hours of the study period. Patients eligible for the study included those who were admitted through an emergency department and those who were already in-patients in a hospital setting, as long as they had acute agitation at the time of patient randomization. This study was the first AZ-004 study enrolling bipolar disorder patients. The primary endpoint for the study was a reduction of agitation, measured as the change from baseline in the PANSS, or Positive and Negative Symptom Scale, Excited Component Score, also known as the PEC score, measured at 2 hours after the first dose. The key secondary endpoint was the Clinical Global Impression-Improvement, or CGI-I, score, measured at 2 hours after the first dose. Both the 5 mg and 10 mg doses of AZ-004 met these primary and secondary endpoints. All results were considered statistically significant at the $p < 0.05$ level, as compared to placebo, and all statistical analyses were made on an intent-to-treat basis. The 10 mg dose of AZ-004 exhibited a rapid onset of effect, with statistically significant reduction in agitation at 10 minutes post-dose, the first time point measure in the study. The reduction of agitation was generally sustained through the 24-hour study period. Various additional assessments of a patient's agitation state were conducted at serial time points using the PEC score over the first 4-hour post-dose time period, with follow-up assessments at the end of the 24-hour study period. Side effects were recorded for each patient throughout the clinical trial period. The administration of AZ-004 was generally safe and well tolerated. The most common side effect, and the only side effect reported by at least 10% of the patients in any treatment group, was taste. This side effect was rated as mild in all patients.

  In September 2008, we announced positive results from the first of our two Phase 3 clinical trials of AZ-004. This trial enrolled 344 acutely-agitated schizophrenic patients at 24 U.S. clinical centers. The trial was designed as an in-clinic, multi-center, randomized, double-blind, placebo-controlled study and tested AZ-004 at two dose levels, 5 mg and 10 mg. Patients were eligible to receive up to 3 doses of study drug in a 24-hour period, depending on their clinical status. The primary endpoint for the study was the change from baseline in the PEC score, measured at 2 hours after the first dose. The key secondary endpoint was the CGI-I score, measured at 2 hours after the first dose. Both the 5 mg and 10 mg doses of AZ-004 met the primary and secondary endpoints. All results were considered statistically significant at the $p < 0.05$ level, as compared to placebo, and all statistical analyses were made on an intent-to-treat basis. The 10 mg dose of AZ-004 exhibited a rapid onset of effect, with statistically significant reductions in agitation at 10 minutes post-dose. The reduction of agitation was generally sustained through the 24-hour study period. Various additional assessments of a patient's agitation state were conducted at serial time points using the PEC scale over the first 4-hour post-dose time period, with follow-up assessments at the end of the 24-hour study period. Side effects were recorded for each patient throughout the clinical trial period. The administration of AZ-004 was generally safe and well tolerated. The most common side effects, reported by at least 10% of the patients in any treatment group, were taste, dizziness, sedation and headache. These side effects were generally mild to moderate in severity.

We have completed five clinical trials with AZ-004, enrolling more than 800 patients, and have announced positive results from these studies. In addition to the two Phase 3 studies outlined above, these trials consist of a 50 subject Phase 1 study in healthy volunteers, a 129 patient Phase 2 study in acutely-agitated schizophrenic patients, and a 32 patient multiple-dose tolerability and pharmacokinetic study in non-agitated schizophrenic patients. We completed an end-of-Phase 2 meeting with the FDA for AZ-004 in September 2007, and we believe we have a clear understanding of the development requirements for filing an NDA for AZ-004.

AZ-004 has been licensed to Symphony Allegro, Inc., or Symphony Allegro, and we have the right to repurchase all rights to this product candidate.

- *AZ-104* (*Staccato* loxapine). We are developing AZ-104 to treat patients suffering from acute migraine headaches. AZ-104 is a lower-dose version of AZ-004. AZ-104 has completed a Phase 2a in-clinic study in migraine patients. In January 2009, we initiated an outpatient, multi-center, randomized, double-blind, single-dose, placebo-controlled study intended to enroll 360 patients who have migraines, with or without aura. Two dose levels of AZ-104 are being evaluated in the clinical trial, 1.25mg and 2.5 mg. The primary efficacy endpoint for the trial is headache pain relief at 2 hours post-dose, using the standard IHS 4-point rating scale. Secondary efficacy endpoints for the trial include pain relief and other symptom assessments at various time points. Safety evaluations will also be made throughout the clinical trial period.

  AZ-104 has been licensed to Symphony Allegro, and we have the right to repurchase all rights to this product candidate.

- *AZ-001 (Staccato* prochlorperazine*).* We are developing AZ-001 to treat patients suffering from acute migraine headaches. During the third quarter of 2008, we conducted an end-of-Phase 2 meeting with the FDA. We believe we have a clear understanding of the development requirements for filing an NDA for this product candidate. We have completed four clinical trials with AZ-001, enrolling 629 patients, and have announced positive results from these studies. These studies consist of a 54 subject Phase 1 study in healthy volunteers, a 75 patient Phase 2a in-clinic study in migraine patients, a 452 patient Phase 2b study in outpatient migraine patients and a 48 subject thorough QT study in healthy volunteers. We do not intend to conduct any AZ-001 Phase 3 studies without a partner, and we are continuing to seek partners for our *Staccato* migraine product candidates, AZ-001 and AZ-104.

- *AZ-007* (*Staccato* zaleplon). We are developing AZ-007 for the treatment of insomnia in patients who have difficulty falling asleep, including patients who awake in the middle of the night and have difficulty falling back asleep. We have completed and announced positive results from a Phase 1 clinical trial of AZ-007. We do not intend to conduct any AZ-007 Phase 2 studies without a partner in 2009.

- *AZ-003* (*Staccato* fentanyl). We are developing AZ-003 for the treatment of patients with acute pain, including patients with breakthrough cancer pain and postoperative patients with acute pain episodes. We have completed and announced positive results from a Phase 1 clinical trial of AZ-003 in opioid naïve healthy subjects.

  In December 2007, we entered into a license, development and supply agreement, or the license agreement, with Endo Pharmaceuticals, Inc, or Endo, for AZ-003 and the fentanyl class of molecules for North America. Under the terms of the license agreement, Endo paid us an upfront fee of $10 million, and was obligated to pay potential additional milestone payments of up to $40 million upon achievement of predetermined regulatory and clinical milestones. Endo was also obligated to pay undisclosed royalties to us on net sales of the product, from which we would be required to pay for the cost of goods for the manufacture of the commercial version of the product. Under the terms of the license agreement, we had the primary responsibility for the development and costs of the *Staccato* Electronic Multiple Dose device and the exclusive right to manufacture the product for clinical development and commercial supply. Endo had the responsibility for future pre-clinical, clinical and regulatory development, and, if AZ-003 was approved for marketing, for commercializing the product in North America. In January 2009, we mutually agreed with Endo to terminate the license agreement with all rights to AZ-003 reverting back to us. We recorded the $10 million upfront fee we received from Endo in January 2008 as deferred revenue and began to recognize

this revenue in the third quarter of 2008 over the estimated performance period of six years, resulting in revenue of $486,000 in 2008. Our obligations under the license agreement were fulfilled upon the termination of the agreement, and we will recognize the remaining deferred revenue in the first quarter of 2009. We do not expect to pursue the development of AZ-003 without a partner.

- *AZ-002 (Staccato* alprazolam*).* AZ-002 has completed a Phase 1 clinical trial in 50 healthy volunteers and a Phase 2a proof-of-concept clinical trial for the treatment of panic attacks, an indication we are not planning to pursue. However, given the safety profile, the successful and reproducible delivery of alprazolam, and the IV-like pharmacological effect demonstrated to date, we and Symphony Allegro are assessing AZ-002 for other possible indications and renewed clinical development. AZ-002 has been licensed to Symphony Allegro, and we have the right to repurchase all rights to this product candidate.

In December 2006, we entered into a transaction involving a series of related agreements providing for the financing of additional clinical and nonclinical development of AZ-002, *Staccato* alprazolam, and AZ-004/AZ-104, *Staccato* loxapine. Pursuant to the agreements, Symphony Capital LLC, a wholly owned subsidiary of Symphony Holdings LLC, and its investors have invested $50 million to form Symphony Allegro to fund additional clinical and nonclinical development of *Staccato* alprazolam and *Staccato* loxapine. We have exclusively licensed to Symphony Allegro certain intellectual property rights related to *Staccato* alprazolam and *Staccato* loxapine. We have retained manufacturing rights to these product candidates. We continue to be primarily responsible for the development of these product candidates in accordance with a development plan and related development budgets, and we have incurred and may continue to incur expenses that are not funded by Symphony Allegro. Pursuant to the agreements, we have received an exclusive purchase option that gives us the right, but not the obligation, to acquire all, but not less than all, of the equity of Symphony Allegro, and reacquire the intellectual property rights that we licensed to Symphony Allegro. This purchase option is exercisable at predetermined prices between $92.5 million at March 1, 2009 and $122.5 million at December 1, 2010. The purchase option exercise price may be paid for in cash or in a combination of cash and our common stock, in our sole discretion, provided that the common stock portion may not exceed 40% of the purchase option exercise price or 10% of our common stock issued and outstanding as of the purchase option closing date. If we pay a portion of the purchase option exercise price in shares of our common stock, then we will be required to register such shares for resale under a resale registration statement pursuant to the terms of a registration rights agreement. If we do not exercise our purchase option by December 1, 2010, then Symphony Allegro will retain its exclusive license to develop and commercialize *Staccato* alprazolam and *Staccato* loxapine for all indications, and we will maintain exclusive rights to manufacture and sell *Staccato* alprazolam and *Staccato* loxapine to Symphony Allegro or its sublicensee for those purposes. Pursuant to a warrant purchase agreement, we issued to Symphony Allegro Holdings, LLC a warrant with a five-year term to purchase 2,000,000 shares of our common stock at $9.91 per share, also paid a transaction structuring fee of $2.5 million, and reimbursed approximately $329,000 of Symphony Allegro transaction fees.

We have retained all other rights to our product candidates and the *Staccato* system. We are seeking a partner in the United States for our lead product candidate, AZ-004, and intend to retain co-promotion rights in the United States. We eventually plan to build a United States-based specialty sales force to commercialize our product candidates which are approved for marketing and which are intended for specialty pharmaceutical markets. We plan to enter into strategic partnerships with other companies to commercialize products that are intended for certain markets in the United States and for all of our product candidates in geographic territories outside the United States.

In March 2008, we obtained a committed equity line of credit under which we may sell, subject to certain limitations, up to $50 million of our registered common stock to Azimuth Opportunity, Ltd., or Azimuth, over a 24-month period. We are not obligated to utilize any of the $50 million equity line of credit. We will determine, at our sole discretion, the timing, the dollar amount and the price per share of each draw under this equity line of credit, subject to certain conditions. When and if we elect to use the equity line of credit, we will issue shares to Azimuth at a discount between 4.15% and 6.00% to the volume weighted average price of our common stock over a preceding period of trading days. Azimuth is not required to purchase any shares at a price below $5.00 per share. Any shares sold under this facility will be sold pursuant to a shelf registration statement declared effective by the Securities and Exchange Commission, or the SEC, on April 16, 2007. We have not sold any shares under this agreement as of December 31, 2008.

In March 2008, we sold 1,250,000 shares of our registered common stock to Biomedical Sciences Investment Fund Pte. Ltd, or Bio*One, at a price of $8.00 per share and issued a warrant to Bio*One to purchase up to $3 million of additional shares of our common stock at an exercise price of $8.00 per share. The agreement contained certain conditions, pursuant to which Bio*One was eligible to receive 135,041 additional shares of our registered common stock and an adjustment to the exercise price of the warrant, which would adjust the effective purchase price paid or payable by Bio*One to $7.22 per share. We did not meet these conditions, and in January 2009 we issued Bio*One 135,041 additional registered shares of our common stock and the warrant's exercise price was automatically adjusted to give Bio*One the right to purchase 415,522 shares at a $7.22 per share exercise price. In addition, we committed to initiate and maintain manufacturing operations in Singapore. The warrant became exercisable only if we terminated operations in Singapore or did not achieve certain performance milestones. In December 2008, we did not achieve a specified performance milestone, at which time the warrant became fully exercisable. All securities sold to Bio*One were sold pursuant to a shelf registration statement declared effective by the SEC on April 16, 2007.

Market Opportunity for Acute and Intermittent Conditions

Acute and intermittent medical conditions are characterized by a rapid onset of symptoms that are temporary and severe, and that occur at irregular intervals, unlike the symptoms of chronic medical conditions that continue at a relatively constant level over time. Approved drugs for the treatment of many acute and intermittent conditions, such as antipsychotics to treat agitation, triptans to treat migraine headaches and benzodiazepines to treat anxiety, are typically delivered either in tablets or by injections. Traditional inhalation technologies are also being developed to treat these conditions. These delivery methods have the following advantages and disadvantages:

- *Oral Tablets.* Oral tablets or capsules are convenient and cost effective, but they generally do not provide rapid onset of action. Oral tablets may require at least one to four hours to achieve peak plasma levels. Also, some drugs, if administered as a tablet or capsule, do not achieve adequate or consistent bioavailability due to the degradation of the drug by the stomach or liver or inability to be absorbed into the bloodstream.

- *Injections.* IV injections provide a rapid onset of action and can sometimes be used to titrate potent drugs with very rapid changes in effect. Titration refers to the ability of a patient to self-administer an initial dose of medication and then determine if the medication is effective; if the medication is effective no further dosing is required. However, if the medication is not yet effective, the patient can administer another dose and repeat this process until the patient determines that the medication has had an adequate effect. However, IV injections generally are administered by trained medical personnel in a medical care setting. Other forms of injections result in an onset of action that is generally substantially slower than IV injection, although often faster than oral administration. All forms of injections are invasive, can be painful to some patients and are often expensive. In addition, many drugs are not water soluble and can be difficult to formulate in an injectable form.

- *Traditional Inhalation.* Traditional dry powder and aerosolized inhalation delivery systems have been designed and used primarily for local delivery of drugs to the respiratory airways, not to the deep lung for rapid systemic drug delivery. Certain recent variants of these systems, however, can provide systemic delivery of drugs, either for the purpose of rapid onset of action or to enable noninvasive delivery of drugs that are not orally bioavailable. Nevertheless, many of these systems have difficulty in generating appropriate drug particle sizes or consistent emitted doses for deep lung delivery. To achieve appropriate drug particle sizes and consistent emitted doses, most traditional inhalation systems require the use of excipients and additives such as detergents, stabilizers and solvents, which may potentially cause toxicity or allergic reactions. Many traditional inhalation devices require patient coordination to deliver the correct drug dose, leading to potentially wide variations in the drug delivered to a patient.

As a result of these limitations, we believe there is a significant unmet medical and patient need for products for the treatment of acute and intermittent conditions that can be delivered in precise amounts, provide rapid therapeutic onset, and are noninvasive and easy to use.

Our Solution: *Staccato* System

Our *Staccato* system rapidly vaporizes an excipient-free drug compound to form a proprietary condensation aerosol that is inhaled and rapidly achieves systemic blood circulation via deep lung absorption. The *Staccato* system consistently creates aerosol particles averaging one to three and one-half microns in size, which is the most appropriate size for deep lung inhalation and absorption into the bloodstream.

We believe our *Staccato* system matches delivery characteristics and product attributes to patient needs for acute and intermittent conditions, and also has the following advantages:

- *Rapid Onset.* The aerosol produced with the *Staccato* system is designed to be rapidly absorbed through the deep lung with a speed of therapeutic onset comparable to an IV injection, generally achieving peak plasma levels of drug in two to five minutes.
- *Ease of Use.* The *Staccato* system is breath actuated, and a patient simply inhales to administer the drug dose. Unlike injections, the *Staccato* system is noninvasive and does not require caregiver assistance. The aerosol produced with the *Staccato* system is relatively insensitive to patient inhalation rates. Unlike many other inhalation technologies, the patient does not need to learn a special breathing pattern. In addition, the *Staccato* device is small and easily portable.
- *Consistent Particle Size and Dose.* The *Staccato* system uses rapid heating of the drug film to create consistent and appropriate particle sizes for deep lung inhalation and absorption into the bloodstream. The *Staccato* system also produces a consistent high emitted dose, regardless of the patient's breathing pattern.
- *Broad Applicability.* We have screened over 400 drugs, and approximately 200 have exhibited initial vaporization feasibility using our *Staccato* system. The *Staccato* system can deliver both water soluble and water insoluble drugs and eliminates the need for excipient and additives such as detergents, stabilizers and solvents, avoiding the side effects that may be associated with the excipient or additives.
- *Design Flexibility.* The *Staccato* system can incorporate lockout and multiple dose features, potentially enhancing safety, convenience of patient titration and a variety of administration regimens.

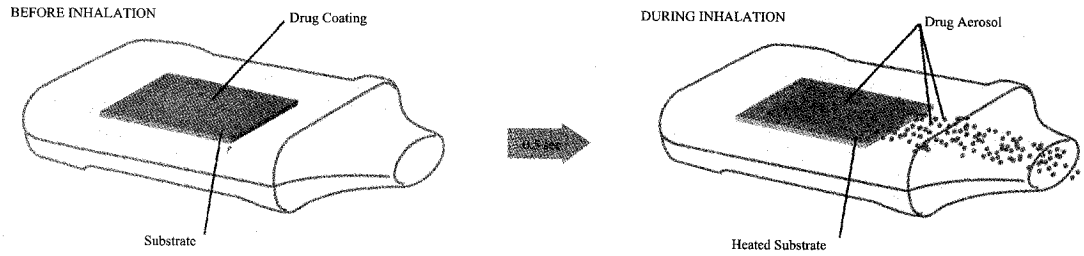
Drug Candidates Based on the Staccato System

We combine small molecule drugs with our *Staccato* system to create proprietary product candidates. We believe that the drugs we are currently using are no longer eligible for patent protection as chemical entities or have their patent protection expiring in the next several years. These drugs have been widely used, and we believe their biological activity and safety are well understood and characterized. We have received composition of matter patent protection on the *Staccato* aerosolized forms of these drugs. We also intend to collaborate with pharmaceutical companies to develop new chemical entities, including compounds that might otherwise not be suitable for development because of limitations of traditional delivery methods.

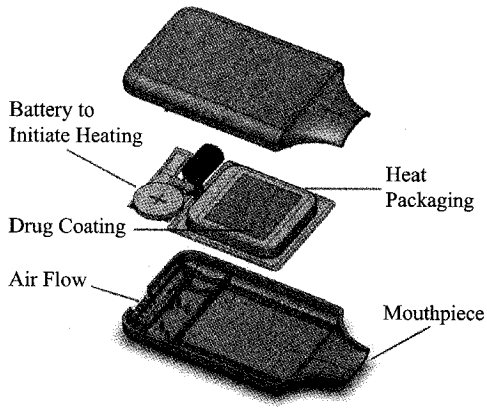
Staccato System

Our product candidates employing *Staccato* system consist of three core components: (1) a heat source that includes an inert metal substrate; (2) a thin film of an excipient-free drug compound (also known as an active pharmaceutical ingredient, or API), coated on the substrate; and (3) an airway through which the patient inhales. The left panel of the illustration below depicts these core components prior to patient inhalation.

The right panel of the illustration below depicts the *Staccato* system during patient inhalation: (1) the heated substrate has reached peak temperature in less than one half second after the start of patient inhalation; (2) the thin drug film has been vaporized; and (3) the drug vapor has subsequently cooled and condensed into excipient-free drug aerosol particles that are being drawn into the patient's lungs. The entire *Staccato* system actuation occurs in less than one second.



Five of our product candidates, AZ-004, AZ-001, AZ-002, AZ-104 and AZ-007, use the same disposable, single dose delivery device. The single dose delivery device consists of a metal substrate that is chemically heated through a battery-initiated reaction of energetic materials. In the current design, the heat package can be coated with up to 10 milligrams of API. The device is portable and easy to carry, with dimensions of approximately three inches in length, two inches in width, and one inch in thickness. The device weighs approximately one ounce. A diagram of the single dose delivery device is shown below:



AZ-003 uses a multiple dose delivery device consisting of a reusable controller and a disposable dose cartridge. We have designed the multiple dose delivery device to meet the specific needs of our AZ-003 product candidate. The dose cartridge currently contains 25 separate metal substrates, each coated with the API, which rapidly heat upon application of electric current from the controller. In the current design, 25 micrograms of drug compound are coated on each metal substrate. The device is portable and easy to carry, with dimensions of approximately five inches in length, two and one-half inches in width and one inch in thickness. The controller weighs approximately four ounces, and the dose cartridge weighs approximately one ounce.

We continue to undertake research and development efforts to improve commercial manufacturability of our single dose device and to develop future generations of the *Staccato* technology.

Our Pipeline

As indicated below, we have one product candidate that is in late-stage Phase 3 clinical testing, one product candidate that has completed Phase 2 clinical testing, two product candidates in Phase 2 clinical testing, and two product candidates that have completed Phase 1 clinical testing.

Product Candidate	API	Target Indication	Status	Alexza Commercial Rights
AZ-004	Loxapine	Acute agitation in schizophrenia or bi-polar disorder patients	Completed pivotal Phase 3 studies	Out-licensed with exclusive repurchase option*
AZ-104	Loxapine	Migraine headaches	Phase 2 on-going	Out-licensed with exclusive repurchase option*
AZ-001	Prochlorperazine	Migraine headaches	Phase 2 completed	Worldwide
AZ-007	Zaleplon	Insomnia	Phase 1 completed	Worldwide
AZ-003	Fentanyl	Acute pain	Phase 1 completed	Worldwide
AZ-002	Alprazolam	Panic attacks	Phase 2 on-going	Out-licensed with exclusive repurchase option*

* Licensed to Symphony Allegro

ACUTE AGITATION PROGRAM: AZ-004 (Staccato loxapine)

We are developing AZ-004 (*Staccato* loxapine) for the acute treatment of agitation in patients with schizophrenia or patients with bipolar disorder. Acute agitation affects many people suffering from major psychiatric disorders, including schizophrenia, which affects approximately 2.4 million adults in the United States, and bipolar disorder, which affects approximately 5.7 million adults in the United States. More than 90% of these patients will experience agitation in their lifetime.

Agitation generally manifests as an escalating series of symptoms. Patients initially feel uncomfortable, tense and restless, and as the agitation intensifies, their behavior becomes more noticeable to others as they become threatening and violent, especially if the agitation is not treated. While patients seek treatment at different points along this agitation continuum, it is individuals exhibiting the most severe symptoms who generally require treatment with injectable drugs in emergency clinical settings — that currently define the acute agitation market. We believe the therapeutic market for agitation is broader than only the limited perspective of patients in crisis, who are in need of rescue intervention.

Our market research indicates that only approximately 50% of treated acute agitation episodes are treated in emergency settings. Another approximately 35% of the treated agitation episodes suffered by schizophrenic and bipolar patients are treated in an inpatient setting (hospital and long-term residential settings), and approximately 15% are treated in a physician's office.

Our market research studies with schizophrenia patient caregivers and bipolar patients indicate these patients, who currently experience acute agitation, average 11 — 12 episodes each year.

Agitation episodes are currently treated about 50% of the time with oral antipsychotics and about 50% of the time with intra-muscular, or IM, injections. Oral medications work relatively slowly, but are easy to administer, painless and are non-threatening to patients. IM injections have a faster onset of action and a higher predictability of drug effect, but because they are invasive and can be frightening to patients, IM injections are usually the treatment option of last-resort.

AZ-004 is an anti-agitation therapeutic that combines Alexza's proprietary *Staccato* system with loxapine, a drug belonging to the class of compounds known generally as antipsychotics. Loxapine is currently approved in oral

and injectable (intramuscular only) formulations in the United States for the management of the manifestations of schizophrenia. The *Staccato* system is a hand-held, chemically-heated, single-dose inhaler that delivers a pure drug aerosol to the highly vascularized tissues of the deep lung.

As an easy-to-use, patient-controlled, and highly reliable therapeutic that provides rapid relief, onset of effect was 10 minutes in two Phase 3 trials, we believe AZ-004 meets the three key treatment attributes for acute agitation specified in the American Association of Emergency Psychiatrists' Expert Consensus Guidelines for the Treatment of Behavioral Emergencies: speed of onset, reliability of medication delivery and patient preference.

We believe that AZ-004, if approved, has the potential to change the treatment paradigm for acutely treating agitation, as the only product able to meet both patient desires for comfort and control, and the clinician goals of rapid and reliable control of an agitation episode.

Development Status

Clinical Trials Phase 3 Clinical Program

Phase 3 — Bipolar Patients

In December 2008, we announced the positive results of our second Phase 3 clinical trial of AZ-004. The clinical trial enrolled 314 acutely-agitated patients with bipolar I disorder at 17 U.S. clinical centers. The trial was designed as an in-clinic, multi-center, randomized, double-blind, placebo-controlled study and tested AZ-004 at two dose levels, 5 mg and 10 mg. Patients were eligible to receive up to 3 doses of study drug in a 24-hour period, depending on their clinical status. Only one dose of study drug was allowed during the first 2 hours of the study period. The primary endpoint for the study was the change from baseline in the PANSS, or Positive and Negative Symptom Scale, Excited Component score, also known as PEC score, measured at 2 hours after the first dose. The key secondary endpoint was the Clinical Global Impression-Improvement, or CGI-I, score, measured at 2 hours after the first dose. All results were considered statistically significant at the $p < 0.05$ level, as compared to placebo, and all statistical analyses were made on an intent-to-treat basis. Various additional assessments of a patient's agitation state were conducted at serial time points using the PEC score over the first 4-hour post-dose time period, with follow-up assessments at the end of the 24-hour study period. Side effects were recorded for each patient throughout their 24-hour study period.

Primary Efficacy Endpoint. Both the 5 mg and the 10 mg dose of AZ-004 met the primary endpoint of the clinical trial, showing a highly statistically significant improvement in the 2-hour post-dose PEC score, compared to placebo.

PEC Scores (Mean Values)

Study Arm	Baseline	2-Hour Post-Dose	p-Value for Change from Baseline vs. Placebo
10 mg AZ-004 (n=105)	17.3	8.3	< 0.0001
5 mg AZ-004 (n=104)	17.4	9.3	<0.0001
Placebo (n=105)	17.7	12.9	—

Key Secondary Efficacy Endpoint. A Clinical Global Impression-Severity, or CGI-S, scale rating of agitation was completed at baseline for each patient, prior to AZ-004 administration, to ensure comparability across groups. The CGI-S scale ranges from 1 (normal) to 7 (among the most extremely agitated patients). Scores were similar across the three dose groups with a range of 4.0 to 4.1. In addition to the PEC score, the Clinical Global Impression-Improvement , or CGI-I, is another commonly used scale to measure the reduction of agitation in patients over time, normally following therapeutic treatment. The CGI-I standard scale ranges from 1 (very much improved) to 7 (very much worse). At the 2-hour post-dose time point, a CGI-I scale rating was completed for each patient, which was the key secondary endpoint of the study. Both the 10 mg and the 5 mg doses of AZ-004 showed statistically significant differences versus placebo in the CGI-I scores at the 2-hour post-dose time point.

CGI-I Scores (Mean Values)

Study Arm	2-Hour Post-Dose	p-Value
10 mg AZ-004 (n=105)	1.9	< 0.0001
5 mg AZ-004 (n=104)	2.1	< 0.0001
Placebo (n=105)	3.0	—

Additional Efficacy Endpoints. The 10 mg dose of AZ-004 also exhibited a rapid onset of effect. At 10 minutes post-dose, the first assessment following dosing, the 10 mg dose showed a highly statistically significant improvement in the PEC score ($p < 0.0001$), compared to placebo. The 10 mg dose sustained this statistically significant improvement at all measurement time points throughout the 24-hour study period, compared to placebo. As pre-specified in the statistical analysis plan, the 5 mg dose was not statistically tested at the time points other than the 2-hour time point.

The duration of the clinical benefit of AZ-004, as measured by the need for additional study drug and /or rescue medication by the 4-hour time point, was significantly different between drug and placebo, and appeared to be dose related. Compared to the 64% of the placebo group that required more than one dose of the study drug and/or rescue medication, 40% of the 5mg group ($p=0.0019$) and only 25% of the 10mg group ($p<0.0001$) required more than one dose of study drug and/or rescue medication. A similar statistically significant pattern was evident for the 24-hour time point.

A responder analysis was conducted using the CGI-I scale. A responder was defined as having a CGI-I score at 2 hours after the first dose of either a 1 (very much improved) or 2 (much improved). Both the 5 mg (66% responders; $p<0.0001$) and 10 mg (74% responders; $p < 0.0001$) doses of AZ-004 were statistically superior to placebo (28% responders).

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 effect, and the only side effect reported by at least 10% of the patients in any treatment group, was taste. This side effect was rated as mild in all patients.

Phase 3 Trial — Schizophrenic Patients

In September 2008, we announced the positive results of the first of our Phase 3 clinical trials of AZ-004. The clinical trial enrolled 344 schizophrenic patients with acute agitation at 24 U.S. clinical centers. The trial was designed as an in-clinic, multi-center, randomized, double-blind, placebo-controlled study and tested AZ-004 at two dose levels, 5 mg and 10 mg. Patients were eligible to receive up to 3 doses of study drug in a 24-hour period, depending on their clinical status. Only one dose of study drug was allowed during the first 2 hours of the study period. The primary endpoint for the study was the change from baseline in the PEC score, measured at 2 hours after the first dose. The key secondary endpoint was the CGI-I, score, measured at 2 hours after the first dose. All results were considered statistically significant at the $p < 0.05$ level, as compared to placebo, and all statistical analyses were made on an intent-to-treat basis. Various additional assessments of a patient's agitation state were conducted at serial time points using the PEC scale over the first 4-hour post-dose time period, with follow-up assessments at the end of the 24-hour study period. Side effects were recorded for each patient throughout their 24-hour study period.

Primary Efficacy Endpoint. Both the 5 mg and the 10 mg dose of AZ-004 met the primary endpoint of the clinical trial, showing a statistically significant improvement in the 2-hour post-dose PEC score, compared to placebo.

PEC Scores (Mean Values)

Study Arm	Baseline	2-Hour Post-Dose	p-Value for Change from Baseline vs. Placebo
10 mg AZ-004 (n=112)	17.6	9.0	< 0.0001
5 mg AZ-004 (n=116)	17.8	9.8	0.0004
Placebo (n=115)	17.4	11.8	—

Key Secondary Efficacy Endpoint. A CGI-S, scale rating of agitation was completed at baseline for each patient, prior to AZ-004 administration, to ensure comparability across groups. The CGI-S scale ranges from 1 (normal) to 7 (among the most extremely agitated patients). Scores were similar across the three dose groups with a range of 3.9 to 4.1. In addition to the PEC score, the CGI-I is another commonly used scale to measure the reduction of agitation in patients over time, normally following therapeutic treatment. The CGI-I standard scale ranges from 1 (very much improved) to 7 (very much worse). At the 2-hour post-dose time point, a CGI-I scale rating was completed for each patient, which was the key secondary endpoint of the study. Both the 10 mg and the 5 mg doses of AZ-004 showed statistically significant differences versus placebo in the CGI-I scores at the 2-hour post-dose time point.

CGI-I Scores (Mean Values)

Study Arm	2-Hour Post-Dose	p-Value
10 mg AZ-004 (n=112)	2.1	< 0.0001
5 mg AZ-004 (n=115)	2.3	0.0015
Placebo (n=115)	2.8	—

Additional Efficacy Endpoints. The 10 mg dose of AZ-004 also exhibited a rapid onset of effect. At 10 minutes post-dose, the 10 mg dose showed a statistically significant improvement in the PEC score ($p < 0.0001$), compared to placebo. The 10 mg dose sustained this statistically significant improvement at all measurement time points throughout the 24-hour study period, compared to placebo.

A dose response pattern for AZ-004 was also apparent, as measured by the need for a patient to require more than one dose of study drug by the 4-hour post-first dose time point. Compared to the 44% of the placebo group that required more than one dose of the study drug, only 25% of the 10 mg group ($p = 0.0039$) and 32% of the 5 mg group ($p = 0.085$) required more than one dose of study drug. A responder analysis was conducted using the CGI-I scale. A responder was defined as having a CGI-I score at 2 hours after the first dose of either a 1 (very much improved) or 2 (much improved). Both the 5 mg (57% responders; $p = 0.0015$) and 10 mg (67% responders; $p < 0.0001$) doses of AZ-004 were statistically superior to placebo (36% responders).

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 by at least 10% of the patients in any treatment group, were taste, dizziness, sedation and headache. These side effects were generally mild to moderate in severity.

Preclinical Studies

Loxapine has been approved for marketing in oral and injectable forms. There are publicly available safety pharmacology, systemic toxicology, carcinogenicity and reproductive toxicology data we will be able to use for our regulatory filings. Therefore, our preclinical development testing is primarily focused on assessing the local tolerability of inhaled loxapine. Our two preclinical inhalation toxicology studies with loxapine have indicated that it was generally well tolerated. We continue to generate the preclinical data that will be required to submit a New Drug Application, or NDA, for AZ-004, which we expect to file in early 2010.

Current Status

In January 2009, we consolidated our operations, with a primary focus on the continued rapid development of AZ-004. We have four supporting clinical studies to complete during 2009 for our AZ-004 NDA. We project that we will complete our clinical studies by the third quarter of 2009 and we project an NDA submission in the first quarter of 2010.

MIGRAINE HEADACHE PROGRAM: AZ-001 (Staccato prochlorperazine) and AZ-104 (Staccato loxapine)

We are developing AZ-001 (*Staccato* prochlorperazine) and AZ-104 (*Staccato* loxapine) for the treatment of acute migraine headaches. Although there are numerous products available for the treatment of migraines,

including simple analgesics such as aspirin and acetaminophen, and nonsteroidal anti-inflammatory drugs such as ibuprofen and naproxen, the prescription market is dominated by a class of orally administered medications commonly known as triptans.

According to the National Headache Foundation, approximately 13 million people in the United States have been diagnosed with migraine headaches and are treated with prescription medications. Acute migraine headaches occur often, usually one to four times a month. Of the estimated 29.5 million migraine sufferers (including diagnosed and undiagnosed sufferers), there are at least two groups of potential patients for whom we believe AZ-001 and AZ-104 could be effective and safe in comparison to triptans. Many migraine sufferers who do take triptans have an insufficient therapeutic response to these medications. In addition, according to the warning labels on triptans, patients with hypertension or high cholesterol, or who smoke cigarettes, are contraindicated for and should not take these medications due to potential cardiovascular and cerebrovascular health risks.

AZ-001 (Staccato prochlorperazine)

The API of AZ-001 is prochlorperazine, a generic drug belonging to the class of drugs known as phenothiazines. Prochlorperazine is currently approved in oral, injectable and suppository formulations in the United States for the treatment of several indications, including nausea and vomiting. In several published clinical studies, 10 mg of prochlorperazine administered intravenously demonstrated effective relief of migraine pain. Prochlorperazine is often administered intravenously to patients with severe migraine headaches who come to emergency departments or migraine treatment clinics. We believe the combination of prochlorperazine with our *Staccato* system could potentially result in a speed of therapeutic onset advantage over oral tablets and a convenience and comfort advantage over injections. In addition, AZ-001 may be appropriate for patients who do not achieve effective relief with triptans or cannot take triptans due to the cardiovascular risk sometimes associated with the administration of triptans. For patients who do not obtain adequate relief from current migraine therapies, AZ-001 may offer a new anti-migraine mechanism of action.

Development Status

Regulatory Status

During the third quarter of 2008, we conducted an end-of-Phase 2 meeting with the FDA. We believe we have a clear understanding of the development requirements for filing an NDA for this product candidate.

Clinical Trials

In December 2007, we completed enrollment of a thorough QT clinical trial, in which two doses of AZ-001 (5 and 10 mg) were compared to active control and to placebo. The purpose of a thorough QT study is to determine a drug's effect on cardiac rhythms. With approximately 40 subjects per study arm, we found that the active control, moxyfloxacin, produced a positive QT/QTc signal that verified the sensitivity of the clinical study. Neither of the doses of AZ-001 produced a QT/QTc prolongation that would suggest an increased risk of cardiac arrhythmia.

We reported initial results of a Phase 2b clinical trial in March 2007. The AZ-001 Phase 2b clinical trial was an outpatient, multi-center, randomized, double blind, placebo-controlled study. The study was designed to evaluate the treatment of a single migraine attack in each of approximately 400 migraine patients, with and without aura. In the trial, three doses of AZ-001 (5 mg, 7.5 mg and 10 mg doses) and placebo were tested, with 100 patients assigned to each treatment group. The primary efficacy endpoint for the trial was headache pain relief at 2-hours post-dose, as defined by the IHS 4-point headache pain rating scale. Secondary efficacy endpoints for the trial included various additional measurements of pain relief, as well as effects on nausea, vomiting, phonophobia and photophobia. The clinical trial study period was 24 hours post dosing for each patient. All results were considered statistically significant at the $p < 0.05$ level, as compared to placebo, and all statistical analyses were made on an intent-to-treat basis. Side effects were recorded throughout the clinical trial study period, and a safety evaluation was made at each patient's closeout visit.

Primary Efficacy Endpoint. AZ-001 met the primary efficacy endpoint of the clinical trial, which was pain relief at 2-hours post-dose using the IHS 4-point headache pain rating scale, for all three doses of the drug compared

to placebo. Statistically significant improvements in pain response were observed in 66.0% of patients at the 10 mg dose (p=0.0013), 63.7% of patients at the 7.5 mg dose (p=0.0046) and 60.2% of patients at the 5 mg dose (p=0.0076), compared to 40.8% of patients receiving placebo.

Additional Efficacy Endpoints. Another measure of efficacy was the achievement of a pain-free response at 2 hours, where a patient has a pain score of 0, or "no", headache pain at the 2-hours post-dose time point. In the trial, AZ-001 showed statistically significant differences from placebo in this measure with 35.0% of patients who received the 10 mg dose achieving pain-free status (p=0.0019) and 29.7% of patients who received the 7.5 mg dose achieving pain-free status (p=0.0226). Patients receiving the 5 mg dose (21.4%) did not achieve a statistically significant pain-free response, compared to placebo. The rate of pain-free response at 2 hours in patients receiving placebo was 15.3%.

We believe duration of efficacy is an important consideration in developing migraine therapeutics. A commonly used measure of duration of efficacy is the sustained pain-free response, whereby a patient reports a pain-free score at the 2-hour post-dose time point and remains pain-free for the remainder of the study period (through 24 hours). The 10 mg and 7.5 mg doses of AZ-001 showed statistically-significant differences in sustained pain-free response, compared to placebo. Sustained pain-free outcomes through 24 hours were observed in 30.1% and 23.1% of patients in the 10 mg and 7.5 mg dose groups, respectively. The placebo group exhibited a sustained pain-free response in 10.2% of patients.

AZ-001 exhibited rapid onset of pain relief. The 7.5 mg dose showed statistically significant pain response, compared to placebo, at 15 minutes (p=0.016). At 30 minutes, all three doses of AZ-001 showed statistically significant pain response, compared to placebo; 10 mg (p=0.0056), 7.5 mg (p=0.0003) and 5 mg (p=0.0056).

Symptom management is an important consideration in the overall efficacy of a migraine therapy. Important symptoms to be managed in migraine patients are nausea, vomiting, photophobia (sensitivity to light) and phonophobia (sensitivity to sound). Survival analyses for nausea, photophobia and phonophobia over the 2 hour time period post-dose showed a statistically significant difference, compared to placebo. The total number of patients with vomiting were too few to make conclusions about drug effect.

Safety Evaluations. Side effects were recorded throughout the clinical trial study period, and a safety evaluation was made at each patient's closeout visit. There were no serious adverse events reported during the trial. The most common side effects reported by at least 10% of the patients in any treatment group were, taste, throat irritation, cough, and somnolence. These side effects appeared to be dose related, with a lower incidence and severity of the side effects generally seen at the lower doses of AZ-001. These side effects were generally mild to moderate in severity.

Preclinical Studies

We have completed several preclinical studies of AZ-001 including inhalation toxicology studies in two animal species, cardiovascular and respiratory safety studies in one species, and *in vitro* and *in vivo* studies to assess potential gene mutations. In animal toxicology studies of prochlorperazine aerosols involving prolonged daily dosing, we detected changes to, and increases in the number of, the cells in the upper airway of the test animals. The terms for these changes and increases are "squamous metaplasia" and "hyperplasia," respectively. We also observed lung inflammation in some animals. Squamous metaplasia and hyperplasia occurred at doses that were substantially greater than those administered in our human clinical trials. In subsequent toxicology studies of AZ-001 involving intermittent dosing, we detected lower incidence and severity of squamous metaplasia and hyperplasia in the upper airway of the test animals compared to the daily dosing results. No lung inflammation was observed with intermittent dosing. During the second quarter of 2008, we completed a 28-day repeat dose inhalation study in dogs. Consistent with previous findings in shorter-term and higher dose studies, we observed dose-related minimal to slight squamous metaplasia in the upper respiratory tract, primarily in the lining of the nasal passages, in all treated groups. These changes were partially reversible by the end of a 28-day post-treatment period. No lower respiratory tract or lung findings were reported. We do not expect to observe these events when AZ-001 is delivered intermittently and at proportionately lower doses in future toxicology studies. We continue to conduct toxicology and other preclinical studies, including preliminary studies to prepare for potentially required longer term carcinogenicity studies, to generate the preclinical data that will be required to submit an NDA for AZ-001.

AZ-104 (Staccato loxapine)

We are developing AZ-104 for the treatment of acute migraine headaches. The API of AZ-104 is loxapine, a generic drug belonging to the class of drugs known as antipsychotics. Loxapine is currently approved in oral and injectable (intramuscular only) formulations in the United States for the management of the manifestations of schizophrenia.

Development Status

Clinical Trials

Phase 2b Clinical Trial

In January 2009, we initiated an outpatient, multi-center, randomized, double-blind, single-dose, placebo-controlled study intended to enroll approximately 360 patients who have migraines, with or without aura. Three doses will be evaluated in the clinical trial, placebo and two doses of AZ-104 (1.25 mg and 2.5 mg). The primary efficacy endpoint for the trial is headache pain relief at 2 hours post-dose, using the standard IHS 4-point rating scale. Secondary efficacy endpoints for the trial include pain relief and other symptom assessments at various time points. Safety evaluations will also be made throughout the clinical trial period.

Phase 2a Clinical Trial

We completed enrollment of a Phase 2a proof-of-concept clinical trial for patients with migraine headache in December 2007 and reported initial results of this trial in March 2008. The Phase 2a clinical trial was an in-clinic, multi-center, randomized, double-blind, single-administration, placebo-controlled study in approximately 160 migraine patients with or without aura. Three doses of AZ-104 (1.25 mg, 2.5 mg and 5 mg) were evaluated against placebo in the clinical trial. Using the IHS 4-point rating scale, the primary efficacy endpoint was pain-relief response at 2 hours post-administration. Secondary efficacy endpoints for the trial included additional pain response assessments and other symptom assessments at various time points. Safety evaluations were made throughout the clinical trial period.

Primary Efficacy Endpoint. AZ-104 met the primary efficacy endpoint of the clinical trial for two doses of the drug compared to placebo. All results were considered statistically significant at the $p < 0.05$ level, as compared to placebo, and all statistical analyses were made on an intent-to-treat basis. Statistically significant improvements in pain response were observed in 76.7% of patients at the 5 mg dose ($p = 0.02$), 79.1% of patients at the 2.5 mg dose ($p = 0.01$) and 67.4% of patients at the 1.25 mg dose ($p = 0.18$), compared to 51.3% of patients receiving placebo. Using survival analysis for pain relief response, all three dose groups were statistically superior ($p < 0.05$) to placebo during the 4-hour post-treatment time period that the patients remained in the clinic.

	Primary Efficacy Endpoint — Pain Relief at 2-Hous Post-Dose			
Treatment	Number of Patients	Patients Achieving Pain Relief	Percent Pain Relief	p-value vs. Placebo
Placebo	39	20	51.3%	na
1.25 mg	43	29	67.4%	0.18
2.5 mg	43	34	79.1%	0.01*
5 mg	43	33	76.7%	0.02*

* Statistically significant results

Additional Efficacy Endpoints. Additional measures of efficacy included the achievement of a pain-free response, in which a patient has a post-dose pain score of 0 (or "no") headache pain. In the trial, AZ-104 showed statistically significant differences from placebo in this measure at the 2-hour time point with 30% of patients achieving pain-free status at the 2.5 mg dose ($p = 0.01$) and 28% at the 1.25 mg dose ($p = 0.02$). While the 5.0 mg dose was numerically superior to placebo with 21% pain-free, this group did not achieve a statistically significant response, compared to placebo ($p = 0.12$). The rate of pain-free response at 2 hours in patients receiving placebo was

8%. Using survival analysis for pain free response, all three dose groups were statistically superior ($p < 0.05$) to placebo during the 4-hour post-treatment time period that the patients remained in the clinic.

A commonly used measure of duration of efficacy is the sustained pain-free response, in which a patient reports a pain-free score at the 2-hour post-dose time point and remains pain-free for the remainder of the study period (up to 24 hours). The 2.5 mg dose of AZ-104 showed a statistically significant difference in sustained pain-free response (26%, $p = 0.04$) compared to placebo (8%). Sustained pain-free outcomes for the 5 mg (16%) and the 1.25 mg (21%) dose groups were not statistically significant.

Important symptoms to be managed in migraine patients are nausea, photophobia (sensitivity to light) and phonophobia (sensitivity to sound). This proof-of-concept trial was not powered to detect differences in these measurements. AZ-104 did exhibit statistically significant improvement in nausea across all dose levels (survival analysis, $p = 0.02$). Positive trends were observed in the improvement of the other symptoms, but the changes were not statistically significant.

Safety Evaluations. Side effects were recorded throughout the clinical trial study period. There were no serious adverse events reported during the trial. The most common side effects, reported by at least 10% of the patients in any treatment group, were taste, somnolence, and fatigue. These side effects were generally mild to moderate in severity.

Preclinical Studies

Loxapine has been approved for marketing in oral and injectable forms. There are publicly available safety pharmacology, systemic toxicology, carcinogenicity and reproductive toxicology data we will be able to use for our regulatory filings. Therefore, our preclinical development testing is primarily focused on assessing the local tolerability of inhaled loxapine. Our two preclinical inhalation toxicology studies with loxapine have indicated that it was generally well tolerated. We continue to conduct toxicology, including extended duration exposure testing, and other preclinical studies to generate the data that will be required to submit an NDA for AZ-104.

INSOMNIA PROGRAM: AZ-007 (Staccato zaleplon)

We are developing AZ-007 for the treatment of insomnia in patients who have difficulty falling asleep, including those patients with middle of the night awakening who have difficulty falling back asleep. Insomnia is the most prevalent sleep disorder, and we believe that it affects at least 15% to 20% of the US population, with some estimates of up to 50% of Americans reporting difficulty getting a good nights' sleep at least a few nights a week. Insomnia can be due to any variety of causes, including depression, grief or stress, menopause, age, shift work, or environmental disruption. Whatever the cause of insomnia, it can take its toll on both the afflicted and the non-afflicted. Sleep disturbances have a major negative impact on public health and economic productivity. Costs for direct healthcare associated with insomnia are estimated to be approximately $14 billion to $15 billion each year.

Market Opportunity

Insomnia is a prevalent disorder that drives almost $5 billion in worldwide sales of prescription medications each year. In a large survey conducted by the National Sleep Foundation in 2005, results showed that 54% of the respondents experienced a minimum of one symptom of insomnia at least a few nights a week. Of those, respondents complained primarily of waking up feeling unrefreshed (38%), waking up frequently during the night (32%), having difficulty falling asleep (21%), and waking up too early and not being able to get back to sleep (21%).

Although benzodiazepines have been the gold standard in treatment for sleep disorders for decades, issues with drug misuse and dependency are common and concerning. Other current treatments for insomnia include non-benzodiazepine GABA-A receptor agonists, which include Ambien (immediate release and controlled-release tablets), Sonata, and Lunesta, which have less abuse potential and side effects than classical benzodiazepines and can be used for longer term treatment. Patients and physicians surveyed suggest that current oral forms of these leading insomnia medications can take from 30-60 minutes to work, while promotions for insomnia medications cite 20-30 minutes. Compounds with a longer half-life that keep patients asleep longer, or those that are dosed in the middle of the night are also those that have residual side effects that can cause a 'hangover' feeling the next day.

We believe the opportunity in insomnia is achieving a balance in treating patients so they can fall asleep quickly (whether at bedtime or in the middle of the night) while enabling them to function well the next day without a groggy feeling. We believe there is a potentially significant clinical need for rapid and predictable onset of sleep in patients with insomnia, coupled with a predictable duration of sleep and rapid, clear awakening that can be satisfied with AZ-007.

Development Status

Clinical Studies

In April 2008, we announced positive results from a Phase 1 clinical trial of AZ-007. The AZ-007 Phase 1 clinical trial enrolled 40 healthy volunteers at a single U.S. clinical center. The purpose of this trial was to assess the safety, tolerability and pharmacokinetic parameters of a single dose of AZ-007. Using a double blind, randomized, dose-escalation trial design, 4 doses of AZ-007 (ranging from 0.5 to 4.0 mg) were compared to placebo.

AZ-007 delivered an IV-like pharmacokinetic profile with a median time to peak venous concentration, or Tmax, of 1.6 minutes. Zaleplon exposure was dose proportional across the 4 doses studied, as calculated by power analysis. Pharmacodynamics, measured as sedation assessed on a 100 mm visual-analog scale, showed onset of effect as early as 2 minutes after dosing with AZ-007.

The most common side effects, reported by at least 10% of the patients in any treatment group, were dizziness and somnolence. These side effects were generally mild to moderate in severity. This data indicated a rapid onset of effect, apparently directly related to the IV-like pharmacokinetics, and showed that AZ-007 was generally safe and well tolerated in this population of healthy volunteers

Preclinical Studies

Zaleplon, the active pharmaceutical ingredient in AZ-007, has been approved for marketing in oral form. There are publicly available safety pharmacology, systemic toxicology, carcinogenicity and reproductive toxicology data we will be able to use for our regulatory filings. Therefore, our preclinical development testing is primarily focused on assessing the local tolerability of inhaled zaleplon. Our two preclinical inhalation toxicology studies with zaleplon have indicated that it was generally well tolerated.

ACUTE PAIN PROGRAM: AZ-003 (Staccato fentanyl)

We are developing our product candidate AZ-003 (*Staccato* fentanyl) for the treatment of patients with acute pain, including patients with breakthrough cancer pain and postoperative patients with acute pain episodes. Based on our analysis of industry data and clinical literature, we believe over 25 million postoperative patients experience inadequate pain relief, despite receiving some form of pain management and, according to a three month study on cancer pain by Portenoy and Hagen (1990) and a cross-sectional study on cancer pain by Caraceni (2004), approximately 65% of patients diagnosed with cancer pain experience breakthrough cancer pain. A patient controlled analgesia, or PCA, IV pump is often used directly after surgery so the patient can achieve quick pain relief as needed. The PCA pump approach generally works well, but typically requires patients to remain in the hospital with an IV line in place. Physicians generally treat cancer pain using a combination of a chronic, long-acting drug and an acute or rapid acting drug for breakthrough pain. Treating a breakthrough pain episode with an oral medication is difficult due to the slow onset of therapeutic effect. However, patients usually also find more invasive, injectable treatments undesirable. Based on preclinical testing and the results of our Phase 1 clinical trial, we believe the PK of fentanyl delivered using a *Staccato* system will be similar to the PK of IV fentanyl administration. We believe many patients would benefit from a noninvasive but fast acting therapy that allows them to titrate the amount of pain medication to the amount of pain relief required.

The API of AZ-003 is fentanyl, a generic drug belonging to the class of drugs known as opioid analgesics. Fentanyl is currently approved in three different formulations in the United States for the management of various types of pain: injectable, transmucosal, which deliver drugs through the mucous membranes of the mouth or nose, and transdermal, which deliver drug through the skin. Since the *Staccato* system can incorporate lockout and multiple dose features, we believe that AZ-003 will facilitate patient titration to the minimum effective drug dose in

a safe, convenient, easy to use and simple delivery system. In addition, we believe the incorporation of patient lockout features may be a significant safety advantage and has the potential to prevent diversion, or use by individuals who have not been prescribed the drug.

Development Status

Clinical Studies

We completed the initial analysis of the top-line results of our Phase 1 clinical trial with AZ-003 in December 2006. The primary aims of the Phase 1 clinical trial were to evaluate the arterial PK and absolute bioavailability for AZ-003 by comparing the AZ-003 profile to that of IV fentanyl, and to examine the pharmacodynamics, tolerability and safety of AZ-003 in opioid naive healthy subjects. The trial enrolled 50 subjects and was conducted at a single clinical center in two stages. Stage 1 of the protocol was an open-label, crossover comparison of a 25 g dose of AZ-003 by a single inhalation and the same dose of fentanyl administered intravenously over five seconds. Stage 2 of the protocol was a randomized double-blind, placebo-controlled, dose escalation of AZ-003 evaluating cumulative doses of 50 g, 100 g, 150 g and 300 g of fentanyl. A 25 g individual dose of fentanyl was inhaled once in Stage 1, or 2, 4 or 6 times at 4 minute intervals for the first four different cohorts in Stage 2. A fifth cohort in Stage 2 received a 150 g dosing sequence starting at time zero and then a second 150 g dosing sequence starting at 60 minutes after the first dose, for a cumulative dose of 300 g. In addition to comprehensive PK sample collection, pharmacodynamic data were generated using pupillometry, a surrogate measure used to assess the functional activity of opioids.

The AZ-003 PK was substantially equivalent to the IV fentanyl PK, with similar peak plasma concentration, or Cmax, time to maximum plasma concentration, or Tmax, and area under the curve concentration, or AUC. These data suggest very high absolute bioavailability of the inhaled dose. Mean peak arterial plasma concentrations were observed within 30 seconds for both administration routes. In Stage 2 of the clinical trial, ascending doses of AZ-003 controlled by the *Staccato* device, exhibited dose-proportionality of fentanyl throughout the dosing range from 50 mcg to 300 mcg, following an AUC analysis. There were no serious adverse events attributable to AZ-003, and the results from the clinical study showed that AZ-003 was generally safe and well tolerated at all doses.

In October 2007, clinical data from the AZ-003 Phase 1 clinical trial were presented in four different presentations at the American Society of Anesthesiologists 2007 Annual Meeting, in San Francisco, California. The four presentations were entitled, "Pharmacokinetic Profiles of Fentanyl Delivered by Intravenous and Inhaled Thermal Aerosol Routes", "Pharmacokinetic Profile of Multiple Doses of Fentanyl Delivered by Inhaled Thermal Aerosol Route", "Pharmacodynamic Response to Fentanyl Delivered by Intravenous and Inhaled Thermal Aerosol Routes" and "Pharmacodynamic Response to Multiple Doses of Fentanyl Delivered by Inhaled Thermal Aerosol Route". This clinical trial demonstrated that the pharmacokinetic profile of AZ-003 in a single breath offers a speed of onset and consistency equivalent to fentanyl administered intravenously over 5 seconds. This clinical trial also demonstrated that the pharmacodynamic profile of AZ-003 in a single breath was comparable to that of fentanyl administered by intravenous administration.

Preclinical Studies

Fentanyl is approved for marketing in injectable, transdermal and transmucosal forms. We are able to use publicly available safety pharmacology, systemic toxicology and reproductive toxicology data for our regulatory filings. Therefore, our preclinical development testing was primarily focused on assessing the local tolerability of inhaled fentanyl. Our two preclinical inhalation toxicology tests in two animal species with fentanyl have indicated that it was generally well tolerated.

AZ-002 (Staccato alprazolam)

We were developing AZ-002 (*Staccato* alprazolam) for the acute treatment of panic attacks associated with panic disorder, a condition characterized by the frequent, unpredictable occurrence of panic attacks. The API of AZ-002 is alprazolam, a generic drug belonging to the class of drugs known as benzodiazepines. Alprazolam is currently approved in oral formulations in the United States for use in the management of anxiety disorder, for the short term relief of symptoms of anxiety, for anxiety associated with depression, and for the treatment of panic disorder with or without agoraphobia, or abnormal fear of being in public places.

Development Status

Clinical Trials

In June 2008, we released the preliminary results from our Phase 2a proof-of-concept clinical trial with AZ-002 in patients with panic disorder. The study did not meet its two primary endpoints, which were the effect of AZ-002 on the incidence of a doxapram-induced panic attack and the effect of AZ-002 on the duration of a doxapram-induced panic attack, both as compared with placebo. There were no serious adverse events in the clinical trial, and AZ-002 was safe and well tolerated in the study patient population.

The AZ-002 Phase 2a clinical trial was an in-clinic, randomized, double-blind, placebo-controlled proof-of-concept evaluation of patients with panic disorder. After an open-label pilot phase, 40 patients were enrolled at 3 U.S. clinical centers, with 20 patients receiving 1 mg AZ-002 and 20 patients receiving Staccato placebo. The primary aim of the clinical trial was to assess the safety and efficacy of a single dose of AZ-002 in treating a pharmacologically-induced panic attack. Two primary endpoints were prospectively defined for the study, one to assess the effect of treatment on the occurrence of a doxapram-induced panic attack of sufficient intensity and a second to assess the effect of treatment on the duration of the doxapram-induced panic attack. Data for these two endpoints were based on the Acute Panic Inventory, a commonly used 22-item self-report questionnaire designed to measure panic-like response to biological challenges or other stressful situations. After receiving training and baseline assessments, all patients in the double-blind phase of the study received a *Staccato* device (randomized to either 1 mg AZ-002 or placebo) and an intravenous administration of doxapram, a respiratory stimulant used to induce a simulated panic attack.

Preclinical Studies

Alprazolam has been approved for marketing in oral tablet form. There are publicly available safety pharmacology, systemic toxicology, carcinogenicity and reproductive toxicology data that we will be able to use for our regulatory filings. Therefore, our preclinical development plan is primarily focused on assessing the local tolerability of inhaled alprazolam. To date, our two preclinical inhalation toxicology studies with inhaled alprazolam have indicated that it is generally well tolerated.

Product Candidate Selection

Since 2004, we have identified five compounds and have successfully filed six INDs for product candidates using our *Staccato* system. In 2009, our primary emphasis is on later stage clinical development of and seeking regulatory approval for our existing product candidates, particularly AZ-004, and not on new product candidate identification. However, we do believe our *Staccato* system is broadly applicable to a large number of medically important small molecule compounds that could be useful in the treatment of acute and intermittent conditions. Since our inception, we have undertaken technical feasibility screening of approximately 400 compounds, which has resulted in the identification of approximately 200 compounds that have demonstrated initial vaporization feasibility.

Once we have established initial vaporization feasibility, we conduct experiments and activities designed to identify viable product candidates. These experiments and activities include calculation of emitted doses, analysis of whether or not the emitted dose would be therapeutic, particle size analyses, early product stability studies and comprehensive medical and market needs assessments. After completion of these experiments and activities, a formal Product Selection Advisory Board, or PSAB, composed of employees and outside experts, is convened to evaluate these data.

After a positive PSAB decision, we initiate preclinical pharmacology and toxicology studies, with the intent of filing an IND upon successful completion of our preclinical studies. During this preclinical period, we also manufacture toxicology study supplies and initiate the manufacturing scale-up to move the product candidate through manufacturing design verification testing and the production of clinical trial materials. We believe that, with the current development status of our single dose device, we can move a compound from initial screening through filing of an IND in 12 to 18 months.

In January 2009, we consolidated our operations, with a primary focus on the continued rapid development of AZ-004. As our efforts will focus on the development of AZ-004, we do not anticipate moving any new product candidates into the clinic in 2009.

Our Strategy

We intend to develop an extensive portfolio of products. Key elements of our strategy include:

- *Focus on Acute and Intermittent Conditions.* We focus our development and commercialization efforts on product candidates based on our *Staccato* system that are intended to address important unmet medical and patient needs in the treatment of acute and intermittent conditions. To meet these needs, we believe that products that provide rapid onset, ease of use, noninvasive administration and, in some cases, patient titration of dosage are required.
- *Establish Strategic Partnerships.* We intend to strategically partner with pharmaceutical and other companies to provide development funding or to address markets that may require a larger sales force, greater marketing resources or specific expertise to maximize the value of some product candidates. We also intend to seek international distribution partners for our product candidates. We may also enter into strategic partnerships with other pharmaceutical companies to combine our *Staccato* system with their proprietary compounds.
- *Retain and Control Product Manufacturing.* We own all manufacturing rights to our product candidates. We intend to internally complete the final manufacture and assembly of our product candidates and any future products, potentially enabling greater intellectual property protection and economic return from our future products. We also believe controlling the final manufacture and assembly reduces the risk of supply interruptions and allows more cost effective manufacturing.

Licensing Collaborations

Symphony Allegro, Inc.

In December 2006, we entered into a transaction involving a series of related agreements providing for the financing of additional clinical and nonclinical development of AZ-002, *Staccato* alprazolam, and AZ-004/104, *Staccato* loxapine. Pursuant to the agreements, Symphony Capital LLC, a wholly owned subsidiary of Symphony Holdings LLC, and its investors have invested $50 million to form Symphony Allegro to fund additional clinical and nonclinical development of *Staccato* alprazolam and *Staccato* loxapine. We have exclusively licensed to Symphony Allegro certain intellectual property rights related to *Staccato* alprazolam and *Staccato* loxapine. We have retained manufacturing rights to these product candidates. We continue to be primarily responsible for the development of these product candidates in accordance with a development plan and related development budgets, and we have incurred and may continue to incur expenses that are not funded by Symphony Allegro. Pursuant to the agreements, we received an exclusive purchase option that gives us the right, but not the obligation, to acquire all, but not less than all, of the equity of Symphony Allegro, and reacquire the intellectual property rights that we licensed to Symphony Allegro. This purchase option is exercisable at predetermined prices between $92.5 million at March 31, 2009 and $122.5 million at December 1, 2010. The purchase option exercise price may be paid for in cash or in a combination of cash and our common stock, in our sole discretion, provided that the common stock portion may not exceed 40% of the purchase option exercise price or 10% of our common stock issued and outstanding as of the purchase option closing date. If we pay a portion of the purchase option exercise price in shares of our common stock, then we will be required to register such shares for resale under a resale registration statement pursuant to the terms of a registration rights agreement. If we do not exercise our purchase option by December 1, 2010, then Symphony Allegro will retain its exclusive license to develop and commercialize *Staccato* alprazolam and *Staccato* loxapine for all indications, and we will maintain exclusive rights to manufacture and sell *Staccato* alprazolam and *Staccato* loxapine to Symphony Allegro or its sublicensee for those purposes. We anticipate we may use a number of financing sources to finance the exercise price of the repurchase option, including but not limited to: issuing debt or equity securities directly to Symphony Allegro, selling debt or equity securities to investors, entering into a partnership agreement for AZ-004, AZ-002, or AZ-104 , and utilizing current cash and securities. We may be unsuccessful in seeking to raise capital to finance the exercise price of the repurchase option.

Endo Pharmaceuticals, Inc.

In December 2007, we entered into a license, development and supply agreement, or the license agreement, with Endo for AZ-003 and the fentanyl class of molecules for North America. Under the terms of the license agreement, Endo paid us an upfront fee of $10 million, and was obligated to pay potential additional milestone payments of up to $40 million upon achievement of predetermined regulatory and clinical milestones. Endo was also obligated to pay undisclosed royalties to us on net sales of the product, from which we would be required to pay for the cost of goods for the manufacture of the commercial version of the product. Under the terms of the license agreement, we had the primary responsibility for the development and costs of the *Staccato* Electronic Multiple Dose device and the exclusive right to manufacture the product for clinical development and commercial supply. Endo had the responsibility for future pre-clinical, clinical and regulatory development, and, if AZ-003 was approved marketing, for commercializing the product in North America. In January 2009, we mutually agreed with Endo to terminate the license agreement, with all rights to AZ-003 reverting back to us. We recorded the $10 million upfront fee we received from Endo in January 2008 as deferred revenue and began to recognize this revenue in the third quarter of 2008 over the estimated performance period of six years, resulting in revenue of $486,000 in 2008. Our obligations under the license agreement were fulfilled upon the termination of the agreement, and we will recognize the remaining deferred revenue in the first quarter of 2009. We do not expect to pursue the development of AZ-003 without a partner.

Research and Development

Research and development expenditures made to advance our product candidates and other research efforts during the last three fiscal years ending December 31, 2008, 2007 and 2006, respectively were as follows (in thousands):

	Year Ended December 31,		
Preclinical and Clinical Development:	**2008**	**2007**	**2006**
AZ-004/104	$26,789	$15,524	$ 6,073
AZ-003	17,070	1,474	3,687
AZ-001	1,151	8,163	9,535
AZ-002	1,898	3,795	3,094
AZ-007	1,773	8,214	2,384
Other preclinical programs	—	—	3,243
Total preclinical and clinical development	48,681	37,170	28,016
Research	12,884	8,475	8,478
Total research and development	$61,565	$45,645	$36,494

Manufacturing

We manufacture our product candidates with components supplied by vendors and with parts manufactured in-house. We believe that manufacturing our product candidates will potentially enable greater intellectual property protection and economies of scale and decrease the risk of supply interruptions.

We outsource the production of some components of our product candidates, including the printed circuit boards and the molded plastic airways. We currently use single source suppliers for these components, as well as for the API used in each of our product candidates. We will outsource the heat packages used in the single dose version of our *Staccato* system device in the future. We do not carry a significant inventory of these components, and establishing additional or replacement suppliers for any of these components may not be accomplished quickly, or at all, and could cause significant additional expense. With the exception of Autoliv ASP Inc., or Autoliv, which will provide chemical heat packages as described below, our suppliers have no contractual obligations to continue to supply us with any of the components necessary to manufacture our product candidates. Any supply interruption from our vendors would limit our ability to manufacture our product candidates and could delay clinical trials for, and regulatory approval of, our product candidates.

On November 2, 2007, we entered into a manufacturing and supply agreement, or the supply agreement, with Autoliv relating to the commercial supply of chemical heat packages that can be incorporated into our single dose *Staccato* device. Autoliv had developed these chemical heat packages for us pursuant to a development agreement between Autoliv and us executed in October 2005. Under the terms of the supply agreement, Autoliv will develop a manufacturing line capable of producing 10 million chemical heat packages a year. We will pay Autoliv $12 million upon the earlier of December 31, 2011 or 60 days after the approval by the FDA of an NDA filed by us. If either party terminates the supply agreement, we will be required to reimburse Autoliv for certain expenses related to the equipment and tooling used in the production and testing of the chemical heat packages up to $12 million. Upon either payment Autoliv will be required to transfer possession and ownership of such equipment and tooling to us.

Autoliv has agreed to manufacture, assemble and test the chemical heat packages solely for us in conformance with our specifications. We will pay Autoliv a specified purchase price, which varies based on annual quantities ordered by us, per chemical heat package delivered. The initial term of the supply agreement expires on December 31, 2012 and may be extended by written mutual consent. The supply agreement provides that during the term of the supply agreement, Autoliv will be our exclusive supplier of chemical heat packages. In addition, the supply agreement grants Autoliv the right to negotiate for the right to supply commercially any second generation chemical heat package, or a second generation product, and provides that we will pay Autoliv certain royalty payments if we manufacture second generation products ourselves or if we obtain second generation products from a third party manufacturer. Upon the expiration or termination of the supply agreement we will also be required, on an ongoing basis, to pay Autoliv certain royalty payments related to the manufacture of the chemical heat packages by us or third party manufacturers.

The supply agreement also contains certain provisions regarding the rights and responsibilities of the parties with respect to manufacturing specifications, forecasting and ordering, delivery arrangements, payment terms, packaging requirements, change orders, intellectual property rights confidentiality and indemnification, as well as certain other customary matters.

The chemical heat packages for our single dose delivery device are manufactured by coating energetic materials on the inside surface of the metal substrate. After inspection and qualification, we assemble the components of our product candidates and coat the exterior of the metal substrate with a thin film of API. We then place the plastic airway around the assembly and package a completed device in a pharmaceutical-grade foil pouch. The controller for our multiple dose delivery design includes the battery power source for heating the individual metal substrates, a microprocessor that directs the electric current to the appropriate metal substrate at the appropriate time, and an icon-based liquid crystal display that shows the number of doses remaining in the dose cartridge and the controller status. We may need to develop additional versions of our devices for future product candidates.

We believe we have developed quality assurance and quality control systems applicable to the design, manufacture, packaging, labeling and storage of our product candidates in compliance with applicable regulations. These systems include extensive requirements with respect to quality management and organization, product design, manufacturing facilities, equipment, purchase and handling of components, production and process controls, packaging and labeling controls, device evaluation, distribution and record keeping.

In 2007, we completed a current good manufacturing practices, or cGMP, compliant pilot manufacturing facility in our new location in Mountain View, California. In November 2007, we received a pharmaceutical manufacturing license from the California State Food and Drug Branch for this facility. We believe this pilot manufacturing facility will have sufficient capacity to manufacture materials for toxicology studies and clinical trial materials for future clinical trials. We also believe that this facility may be sufficient to manufacture early commercial-scale batches of our products. In February 2008, we completed the move from Palo Alto to our new Mountain View facilities. In January 2009, we renewed our pharmaceutical manufacturing license from the California State Food and Drug Branch for our Mountain View facility. This new license is valid until January 31, 2011.

Product Commercialization

We have conducted a comprehensive strategic marketing review and developed our initial product launch strategy for our lead program, AZ-004, *Staccato* loxapine for the acute treatment of agitation in schizophrenic and bipolar patients. Based on this review, we believe that we will need a partner to initially address the United States market for this product candidate, but plan to also retain co-promotion rights in the United States for this product candidate. Eventually, we plan to build a United States specialty sales force to commercialize any of our product candidates that are approved and are intended for the specialty pharmaceutical type markets. We plan to enter into strategic partnerships with other companies to commercialize products that are intended for other markets in the United States and for all of our product candidates in geographic territories outside the United States.

Government Regulation

The testing, manufacturing, labeling, advertising, promotion, distribution, export and marketing of our product candidates are subject to extensive regulation by governmental authorities in the United States and other countries. Our product candidates include drug compounds incorporated into our delivery device and are considered "combination products" in the United States. We have agreed with the FDA that our product candidates will be reviewed by the FDA's Center for Drug Evaluation and Research. The FDA, under the Federal Food, Drug and Cosmetic Act, or FDCA, regulates pharmaceutical products in the United States. The steps required before a drug may be approved for marketing in the United States generally include:

- preclinical laboratory studies and animal tests;
- the submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials commence;
- adequate and well controlled human clinical trials to establish the safety and efficacy of the product;
- the submission to the FDA of an NDA;
- satisfactory completion of an FDA inspection of the manufacturing facilities at which the product is made to assess compliance with cGMP. In addition, the FDA may audit clinical trial sites that generated the data in support of the NDA; and
- FDA review and approval of the NDA.

The testing and approval process requires substantial time, effort and financial resources, and the receipt and timing of any approval is uncertain. Preclinical studies include laboratory evaluations of the product candidate, as well as animal studies to assess the potential safety and efficacy of the product candidate. The results of the preclinical studies, together with manufacturing information and analytical data, are submitted to the FDA as part of the IND, which must become effective before clinical trials may be commenced. The IND will become effective automatically 30 days after receipt by the FDA, unless the FDA raises concerns or questions about the conduct of the trials as outlined in the IND prior to that time. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can proceed.

Clinical trials involve the administration of the product candidates to healthy volunteers or patients under the supervision of a qualified principal investigator. Further, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical trial will be conducted. The IRB will consider, among other things, ethical factors, the safety of human subjects and the possible liability of the institution.

Clinical trials typically are conducted in three sequential phases prior to approval, but the phases may overlap. A fourth, or post-approval, phase may include additional clinical studies. These phases generally include the following:

- *Phase 1.* Phase 1 clinical trials involve the initial introduction of the drug into human subjects, frequently healthy volunteers. These studies are designed to determine the metabolism and pharmacologic actions of the drug in humans, the adverse effects associated with increasing doses and, if possible, to gain early

evidence of effectiveness. In Phase 1 clinical trials, the drug is usually tested for safety, including adverse effects, dosage tolerance, absorption, distribution, metabolism, excretion and pharmacodynamics.

- *Phase 2.* Phase 2 clinical trials usually involve studies in a limited patient population to (1) evaluate the efficacy of the drug for specific, targeted indications; (2) determine dosage tolerance and optimal dosage; and (3) identify possible adverse effects and safety risks. Although there are no statutory or regulatory definitions for Phase 2a and Phase 2b, Phase 2a is commonly used to describe a Phase 2 clinical trial evaluating efficacy, adverse effects and safety risks and Phase 2b is commonly used to describe a subsequent Phase 2 clinical trial that also evaluates dosage tolerance and optimal dosage.

- *Phase 3.* If a compound is found to be potentially effective and to have an acceptable safety profile in Phase 2 clinical trials, the clinical trial program will be expanded to further demonstrate clinical efficacy, optimal dosage and safety within an expanded patient population at geographically dispersed clinical trial sites. Phase 3 clinical trials usually include several hundred to several thousand patients.

- *Phase 4.* Phase 4 clinical trials are studies required of, or agreed to, by a sponsor that are conducted after the FDA has approved a product for marketing. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of drugs approved under accelerated approval regulations. If the FDA approves a product while a company has ongoing clinical trials that were not necessary for approval, a company may be able to use the data from these clinical trials to meet all or part of any Phase 4 clinical trial requirement. These clinical trials are often referred to as Phase ¾ post-approval clinical trials. Failure to promptly conduct Phase 4 clinical trials could result in withdrawal of approval for products approved under accelerated approval regulations.

In the case of products for the treatment of severe or life threatening diseases, the initial clinical trials are sometimes conducted in patients rather than in healthy volunteers. Since these patients are already afflicted with the target disease, it is possible that such clinical trials may provide evidence of efficacy traditionally obtained in Phase 2 clinical trials. These trials are referred to frequently as Phase 1/2 clinical trials. The FDA may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

The results of preclinical studies and clinical trials, together with detailed information on the manufacture and composition of the product, are submitted to the FDA in the form of an NDA requesting approval to market the product. Generally, regulatory approval of a new drug by the FDA may follow one of three routes. The most traditional of these routes is the submission of a full NDA under Section 505(b)(1) of the FDCA. A second route, which is possible where an applicant chooses to rely in part on the FDA's conclusion about the safety and effectiveness of previously approved drugs is to submit a more limited NDA described in Section 505(b)(2) of the FDCA. The final route is the submission of an Abbreviated New Drug Application for products that are shown to be therapeutically equivalent to previously approved drug products as permitted under Section 505(j) of the FDCA. We do not expect any of our product candidates to be submitted under Section 505(j). Both Section 505(b)(1) and Section 505(b)(2) applications are required by the FDA to contain full reports of investigations of safety and effectiveness. However, in contrast to a traditional NDA submitted pursuant to Section 505(b)(1) in which the applicant submits all of the data demonstrating safety and effectiveness, we believe an application submitted pursuant to Section 505(b)(2) can rely upon findings by the FDA that the parent drug is safe and effective in that indication. As a consequence, the preclinical and clinical development programs leading to the submission of an NDA under Section 505(b)(2) may be less expensive to carry out and can be concluded in a shorter period of time than programs required for a Section 505(b)(1) application. In its review of any NDA submissions, however, the FDA has broad discretion to require an applicant to generate additional data related to safety and efficacy, and it is impossible to predict the number or nature of the studies that may be required before the FDA will grant approval. Notwithstanding the approval of many products by the FDA pursuant to Section 505(b)(2), over the last few years certain brand-name pharmaceutical companies and others have objected to the FDA's interpretation of Section 505(b)(2). If the FDA changes its interpretation of Section 505(b)(2), this could delay or even prevent the FDA from approving any Section 505(b)(2) NDA that we submit.

To the extent that a Section 505(b)(2) applicant is relying on the FDA's findings for an already-approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the

FDA's Orange Book publication. A certification that the new product will not infringe the already approved products' Orange Book-listed patents or that such patents are invalid is called a paragraph IV certification, and could be challenged in court by the patent owner or holder of the application of the already approved products. This could delay the approval of any Section 505(b)(2) application we submit. In addition, any period of marketing exclusivity applicable to the already approved product might delay approval of any Section 505(b)(2) application we submit. Any Section 505(b)(1) or Section 505(b)(2) application we submit for a drug product containing a previously approved API might be eligible for three years of marketing exclusivity, provided new clinical investigations that were conducted or sponsored by the applicant are essential to the FDA's approval of the application. Five years of marketing exclusivity is granted if FDA approves an NDA for a new chemical entity. In addition, we can list in the FDA's Orange Book publication any of our patents claiming the drug product, drug substance or that cover an approved method-of-use. In order for a generic applicant to rely on the FDA's approval of any NDA we submit, such generic applicant must certify to any Orange Book listed patents and might be subject to any marketing exclusivity covering our approved drug product.

In the NDA submissions for our product candidates that are currently undergoing clinical trials, we intend to follow the development pathway permitted under the FDCA that we believe will maximize the commercial opportunities for these product candidates. We are currently pursuing the Section 505(b)(2) application route for our product candidates. As such, we intend to engage in discussions with the FDA to determine which, if any, portions of our development program can be modified, based on previous FDA findings of a drug's safety and effectiveness.

Before approving an NDA, the FDA will inspect the facilities at which the product is manufactured, whether ours or our third party manufacturers', and will not approve the product unless the manufacturing facility complies with cGMP. The FDA reviews all NDA's submitted before it accepts them for filing and may request additional information rather than accept an NDA for filing. Once the NDA submission has been accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, the FDA has 10 months in which to complete its initial review of a standard NDA and respond to the applicant, and six months for a priority NDA. The FDA does not always meet the PDUFA goal dates for standard and priority NDA's. The review process is often significantly extended by FDA requests for additional information or clarification. The FDA may delay approval of an NDA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product. FDA approval of any NDA submitted by us will be at a time the FDA chooses. Also, if regulatory approval of a product is granted, such approval may entail limitations on the indicated uses for which such product may be marketed. Once approved, the FDA may withdraw the product approval if compliance with pre and post-marketing regulatory requirements and conditions of approvals are not maintained or if problems occur after the product reaches the marketplace. In addition, the FDA may require post-marketing studies, referred to as Phase 4 clinical trials, to monitor the effect of approved products and may limit further marketing of the product based on the results of these post-marketing studies.

If we obtain regulatory approval for a product, this approval will be limited to those diseases and conditions for which the product is effective, as demonstrated through clinical trials. Even if this regulatory approval is obtained, a marketed product, its manufacturer and its manufacturing facilities are subject to continual review and periodic inspections by the FDA and, in our case, the State of California. Discovery of previously unknown problems with a medicine, device, manufacturer or facility may result in restrictions on the marketing or manufacturing of an approved product, including costly recalls or withdrawal of the product from the market. The FDA has broad post-market regulatory and enforcement powers, including the ability to suspend or delay issuance of approvals, seize or recall products, withdraw approvals, enjoin violations and institute criminal prosecution.

In addition to regulation by the FDA and certain state regulatory agencies, the United States Drug Enforcement Administration, or DEA, imposes various registration, recordkeeping and reporting requirements, procurement and manufacturing quotas, labeling and packaging requirements, security controls and a restriction on prescription refills on certain pharmaceutical products under the Controlled Substances Act. A principal factor in determining the particular requirements, if any, applicable to a product is its actual or potential abuse profile. The DEA regulates drug substances as Schedule I, II, III, IV or V substances, with Schedule I and II substances considered to present the highest risk of substance abuse and Schedule V substances the lowest risk. Alprazolam, the API in AZ-002, is regulated as a Schedule IV substance, fentanyl, the API in AZ-003, is regulated as a Schedule II substance, and

zaleplon, the API in AZ-007, is regulated as a Schedule IV substance. Each of these product candidates are subject to DEA regulations relating to manufacturing, storage, distribution and physician prescription procedures, and the DEA regulates the amount of the scheduled substance that would be available for clinical trials and commercial distribution. As a Schedule II substance, fentanyl is subject to additional controls, including quotas on the amount of product that can be manufactured and limitations on prescription refills. We have received necessary registrations from the DEA for the manufacture of AZ-002, AZ-003 and AZ-007. The DEA periodically inspects facilities for compliance with its rules and regulations. Failure to comply with current and future regulations of the DEA could lead to a variety of sanctions, including revocation, or denial of renewal, of DEA registrations, injunctions, or civil or criminal penalties, and could harm our business and financial condition.

The single dose design of our *Staccato* system uses what we refer to as "energetic materials" to generate the rapid heating necessary for vaporizing the drug while avoiding degradation. Manufacture of products containing these types of materials is controlled by the Bureau of Alcohol, Tobacco, Firearms and Explosives, or ATF, under 18 United States Code Chapter 40. Technically, the energetic materials used in our *Staccato* system are classified as "low explosives," and we have been granted a license/permit by the ATF for the manufacture of such low explosives.

Additionally, due to inclusion of the energetic materials in our *Staccato* system, shipments of the single dose design of our *Staccato* system are regulated by the Department of Transportation, or DOT, under Section 173.56, Title 49 of the United States Code of Federal Regulations. The single dose version of our *Staccato* device has been granted "Not Regulated as an Explosive" status by the DOT.

We have received funding for one or more research projects from a funding agency of the United States government, and inventions conceived or first actually reduced to practice during the performance of the research project are subject to the rights and limitations of certain federal statutes and various implementing regulations known generally and collectively as the "Bayh-Dole Requirements." As a funding recipient, we are subject to certain invention reporting requirements, and certain limitations are placed on assignment of the invention rights. In addition, the federal government retains a non-exclusive, irrevocable, paid-up license to practice the invention and, in exceptional cases, the federal government may seek to take title to the invention.

We also will be subject to a variety of foreign regulations governing clinical trials and the marketing of any future products. Outside the United States, our ability to market a product depends upon receiving a marketing authorization from the appropriate regulatory authorities. The requirements governing the conduct of clinical trials, marketing authorization, pricing and reimbursement vary widely from country to country. In any country, however, we will only be permitted to commercialize our products if the appropriate regulatory authority is satisfied that we have presented adequate evidence of safety, quality and efficacy. Whether or not FDA approval has been obtained, approval of a product by the comparable regulatory authorities of foreign countries must be obtained prior to the commencement of marketing of the product in those countries. The time needed to secure approval may be longer or shorter than that required for FDA approval. The regulatory approval and oversight process in other countries includes all of the risks associated with the FDA process described above.

Pharmaceutical Pricing and Reimbursement

In both domestic and foreign markets, our ability to commercialize successfully and attract strategic partners for our product candidates depends in significant part on the availability of adequate coverage and reimbursement from third-party payors, including, in the United States, governmental payors such as the Medicare and Medicaid programs, managed care organizations, and private health insurers. Third-party payors are increasingly challenging prices charged for medical products and services and examining their cost effectiveness, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost effectiveness of any future products. Even with studies, our product candidates may be considered less safe, less effective or less cost effective than existing products, and third-party payors therefore may not provide coverage and reimbursement for our product candidates, in whole or in part.

Political, economic and regulatory influences are subjecting the healthcare industry in the United States to fundamental changes. There have been, and we expect there will continue to be, a number of legislative and regulatory proposals to change the healthcare system in ways that could significantly affect our business. We

anticipate that Congress, state legislatures and the private sector will continue to consider and may adopt healthcare policies intended to curb rising healthcare costs. These cost containment measures include:

- controls on government funded reimbursement for medical products and services;
- controls on healthcare providers;
- challenges to the pricing of medical products and services or limits or prohibitions on reimbursement for specific products and therapies through other means;
- reform of drug importation laws; and
- expansion of use of managed care systems in which healthcare providers contract to provide comprehensive healthcare for a fixed cost per person.

We are unable to predict what additional legislation, regulations or policies, if any, relating to the healthcare industry or third-party coverage and reimbursement may be enacted in the future or what effect such legislation, regulations or policies would have on our business. Any cost containment measures, including those listed above, or other healthcare system reforms that are adopted could have a material adverse effect on our ability to operate profitably.

Patents and Proprietary Rights

We actively seek to patent the technologies, inventions and improvements we consider important to the development of our business. In addition, we rely on trade secrets and contractual arrangements to protect our proprietary information. Some areas for which we seek patent protection include:

- the *Staccato* system and its components;
- methods of using the *Staccato* system;
- the aerosolized form of drug compounds produced by the *Staccato* system; and
- methods of making and using the drug containing aerosols, including methods of administering the aerosols to a patient.

As of February 1, 2009, we held over 230 issued and allowed U.S. and international patents. Most of our patents are directed to compositions for delivery of an aerosol comprising drugs other than our lead product candidates described below, and cover the process for producing these aerosols using the *Staccato* system. As of that date, we held over 34 additional pending patent applications in the United States. We also hold over 105 pending corresponding foreign patent applications or Patent Cooperation Treaty applications that will permit us to pursue additional patents outside of the United States. The claims in these various patents and patent applications are directed to various aspects of our drug delivery devices and their components, methods of using our devices, drug containing aerosol compositions and methods of making and using such compositions.

AZ-004/AZ-104 (Staccato loxapine)

One of our issued U.S. patents covers compositions for delivery of a condensation aerosol comprising loxapine and covers the process for producing such condensation aerosol using the *Staccato* system technology. This patent will not expire until 2022. Counterparts to this patent are pending in a number of foreign jurisdictions, including Europe. We also have three other U.S. patents directed to condensation aerosol compositions for delivery of loxapine, kits containing devices for forming such compositions and methods of administering such compositions.

AZ-001 (Staccato prochlorperazine)

One of our issued U.S. patents covers compositions for delivery of a condensation aerosol comprising prochlorperazine and covers the process for producing such condensation aerosol using the *Staccato* system technology. This patent will not expire until 2022. Counterparts to this patent are pending in a number of foreign jurisdictions, including Europe. We also have three other U.S. patents directed to condensation aerosol

compositions for delivery of prochlorperazine, kits containing devices for forming such compositions, and methods of administering such compositions.

AZ-003 (Staccato fentanyl)

One of our issued U.S. patents covers compositions for delivery of a condensation aerosol comprising fentanyl and covers the process for producing such condensation aerosol using the *Staccato* system technology. This patent will not expire until 2022. Counterparts to this patent are pending in a number of foreign jurisdictions, including Europe. We also have three other U.S. patents directed to condensation aerosol compositions for delivery of fentanyl, kits containing devices for forming such compositions, and methods of administering such compositions.

AZ-007 (Staccato zaleplon)

One of our issued U.S. patents covers compositions for delivery of a condensation aerosol comprising zaleplon and covers the process for producing such condensation aerosol using the *Staccato* system technology. This patent will not expire until 2022. Counterparts to this patent are pending in a number of foreign jurisdictions, including Europe. We also have three other U.S. patents directed to condensation aerosol compositions for delivery of zaleplon, kits containing devices for forming such compositions, and methods of administering such compositions.

AZ-002 (Staccato alprazolam)

One of our issued U.S. patents covers compositions for delivery of a condensation aerosol comprising alprazolam and covers the process for producing such condensation aerosol using the *Staccato* system technology. This patent will not expire until 2022. Counterparts to this patent are pending in a number of foreign jurisdictions, including Europe. We also have three other U.S. patents directed to condensation aerosol compositions for delivery of alprazolam, kits containing devices for forming such compositions, and methods of administering such compositions.

Competition

The pharmaceutical and biotechnology industries are intensely competitive. Many pharmaceutical companies, biotechnology companies, public and private universities, government agencies and research organizations are actively engaged in research and development of products targeting the same markets as our product candidates. Many of these organizations have substantially greater financial, research, drug development, manufacturing and marketing resources than we have. Large pharmaceutical companies in particular have extensive experience in clinical testing and obtaining regulatory approvals for drugs. Our ability to compete successfully will depend largely on our ability to:

- develop products that are superior to other products in the market;
- attract and retain qualified scientific, product development and commercial personnel;
- obtain patent and/or other proprietary protection covering our future products and technologies;
- obtain required regulatory approvals; and
- successfully collaborate with pharmaceutical and biotechnology companies in the development and commercialization of new products.

We expect any future products we develop to compete on the basis of, among other things, product efficacy and safety, time to market, price, extent of adverse side effects experienced and convenience of treatment procedures. One or more of our competitors may develop products based upon the principles underlying our proprietary technologies earlier than we do, obtain approvals for such products from the FDA more rapidly than we do or develop alternative products or therapies that are safer, more effective and/or more cost effective than any future products developed by us. In addition, our ability to compete may be affected if insurers and other third-party payors encourage the use of generic products through other routes of administration, making our pulmonary delivery products less attractive from a cost perspective.

Any future products developed by us would compete with a number of alternative drugs and therapies, including the following:

- AZ-004 would compete with the injectable form of loxapine (Loxitane®) and other antipsychotic drugs, such as Zyprexa® Geodon® and Abilify®;
- AZ-001 and AZ-104 would compete with available triptan drugs, such as Imitrex®, Zomig® and Maxalt®, and IV prochlorperazine;
- AZ-003 would compete with injectable and other forms of fentanyl and various generic oxycodone, hydrocodone and morphine products; and
- AZ-007 would compete with non-benzodiazepine GABA-A receptor agonists, which include Ambien® (immediate release and controlled-release tablets), Sonata®, and Lunesta®.

Many of these existing drugs have substantial current sales and long histories of effective and safe use. As patent protection expires for these drugs, we will also compete with their generic versions. In addition to currently marketed drugs and their generic versions, we believe there are a number of drug candidates in clinical trials that, if approved in the future, would compete with any future products we may develop.

Employees

In January 2009, we consolidated our operations, with a primary focus on the continued rapid development of AZ-004 (*Staccato* loxapine). The restructuring included a workforce reduction of 52 employees, representing approximately 33% of our total workforce.

As of February 28, 2009, we had 111 full time employees, 18 of whom held Ph.D. or M.D. degrees and 82 of whom were engaged in full time research and development activities. None of our employees are represented by a labor union, and we consider our employee relations to be good.

Corporate Information

We were incorporated in the state of Delaware on December 19, 2000 as FaxMed, Inc. In June 2001, we changed our name to Alexza Corporation and in December 2001 we became Alexza Molecular Delivery Corporation. In July 2005, we changed our name to Alexza Pharmaceuticals, Inc.

Available Information

Our website address is www.alexza.com; however, information found on, or that can be accessed through, our website is not incorporated by reference into this Annual Report. We file electronically with the SEC our Annual Report, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934. We make available free of charge on or through our website copies of these reports as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The SEC maintains an internet site that contains reports, proxy and information statements and other information regarding our filings at www.sec.gov. You may also read and copy any of our materials filed with the SEC at the SEC's Public References Room at 100 F Street, NW, Washington, DC 20549. Information regarding the operation of the Public Reference Room can be obtained by calling the SEC at 1-800-SEC-0330.

Item 1A. ***Risk Factors***

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, together with all of the other information included in this Annual Report, before deciding whether to invest in shares of our common stock. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations. The occurrence of any of the following risks could harm our business, financial condition or results of operations. In such case, the trading price of our common stock could decline, and you may lose all or part of your investment.

Risks Relating to Our Business

We have a history of net losses. We expect to continue to incur substantial and increasing net losses for the foreseeable future, and we may never achieve or maintain profitability.

We are not profitable and have incurred significant net losses in each year since our inception, including net losses of $58.5 million, $45.1 million, and $41.8 million for the years ended December 31, 2008, 2007 and 2006, respectively. As of December 31, 2008, we had a deficit accumulated during development stage of $222.5 million. We expect our expenses to decrease in 2009 as a result of our reduction in force which we effected in January 2009; however, we expect to incur substantial net losses and negative cash flow for the foreseeable future. These losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity (deficit) and working capital.

Because of the numerous risks and uncertainties associated with pharmaceutical product development and commercialization, we are unable to accurately predict the timing or amount of future expenses or when, or if, we will be able to achieve or maintain profitability. Currently, we have no products approved for commercial sale, and to date we have not generated any product revenue. We have financed our operations primarily through the sale of equity securities, capital lease and equipment financing and government grants. The size of our future net losses will depend, in part, on the rate of growth of our expenses and the level and rate of growth, if any, of our revenues. Revenues from strategic partnerships are uncertain because we may not enter into any additional strategic partnerships. We began to recognize revenues from our partnership with Endo in the third quarter of 2008, and we will recognize approximately $9.5 million in revenue in the first quarter of 2009 as a result of termination of the Endo agreement in January 2009. However we do not expect to recognize any product or grant revenues in 2009. If we are unable to develop and commercialize one or more of our product candidates or if sales revenue from any other product candidate that receives marketing approval is insufficient, we will not achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability.

We are a development stage company. Our success depends substantially on our lead product candidates. If we do not develop commercially successful products, we may be forced to cease operations.

You must evaluate us in light of the uncertainties and complexities affecting a development stage pharmaceutical company. We have not completed clinical development for any of our product candidates. Each of our product candidates is at an early stage of development and will be unsuccessful if it:

- does not demonstrate acceptable safety and efficacy in preclinical studies and clinical trials or otherwise does not meet applicable regulatory standards for approval;
- does not offer therapeutic or other improvements over existing or future drugs used to treat the same or similar conditions;
- is not capable of being produced in commercial quantities at an acceptable cost, or at all; or
- is not accepted by patients, the medical community or third party payors.

Our ability to generate product revenue in the future is dependent on the successful development and commercialization of our product candidates. We have not proven our ability to develop and commercialize

products. Problems frequently encountered in connection with the development and utilization of new and unproven technologies and the competitive environment in which we operate might limit our ability to develop commercially successful products. We do not expect any of our current product candidates to be commercially available before 2011, if at all. If we are unable to make our product candidates commercially available, we will not generate product revenues, and we will not be successful.

We will need substantial additional capital in the future. If additional capital is not available, we will have to delay, reduce or cease operations.

We will need to raise additional capital to fund our operations, to develop our product candidates and to develop our manufacturing capabilities. Our future capital requirements will be substantial and will depend on many factors including:

- the scope, rate of progress, results and costs of our preclinical studies, clinical trials and other research and development activities, and our manufacturing development and commercial manufacturing activities;
- the amount and timing of payments from Symphony Allegro related to the development of *Staccato* alprazolam and *Staccato* loxapine;
- the amount and timing of any payments to Symphony Allegro related to the repurchase of rights to *Staccato* alprazolam and *Staccato* loxapine;
- our ability to draw on our equity line of credit with Azimuth;
- the cost, timing and outcomes of regulatory proceedings;
- the cost and timing of developing sales and marketing capabilities prior to receipt of any regulatory approval of our product candidates;
- the cost and timing of developing manufacturing capacity;
- revenues received from any future products;
- payments received under any future strategic partnerships;
- the filing, prosecution and enforcement of patent claims; and
- the costs associated with commercializing our product candidates, if they receive regulatory approval.

We believe that with current cash, cash equivalents and marketable securities along with interest earned thereon, expected payments from Symphony Allegro, the proceeds from option exercises, and purchases of common stock pursuant to our Employee Stock Purchase Plan, we will be able to maintain our currently planned operations into the second quarter of 2010. Changing circumstances may cause us to consume capital significantly faster or slower than we currently anticipate. We have based these estimates on assumptions that may prove to be wrong, and we could utilize our available financial resources sooner than we currently expect. The key assumptions underlying these estimates include:

- we do not use our currently available funds to repurchase rights from Symphony Allegro;
- expenditures related to continued preclinical and clinical development of our lead product candidates during this period within budgeted levels;
- the timing and amount of payments from Symphony Allegro;
- no unexpected costs related to the development of our manufacturing capability; and
- no growth in the number of our employees during this period.

We may never be able to generate a sufficient amount of product revenue to cover our expenses. Until we do, we expect to finance our future cash needs through public or private equity offerings, debt financings, strategic partnerships or licensing arrangements, as well as interest income earned on cash and marketable securities balances and proceeds from stock option exercises and purchases under our Employee Stock Purchase Plan. Any

financing transaction may contain unfavorable terms. If we raise additional funds by issuing equity securities, our stockholders' equity will be diluted. If we raise additional funds through strategic partnerships, we may be required to relinquish rights to our product candidates or technologies, or to grant licenses on terms that are not favorable to us.

Unstable market conditions may have serious adverse consequences on our business.

The recent economic downturn and market instability has made the business climate more volatile and more costly. Our general business strategy may be adversely affected by unpredictable and unstable market conditions. If the current equity and credit markets deteriorate further, or do not improve, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. While we believe we have adequate capital resources to meet current working capital and capital expenditure requirements until at least the second quarter of 2010, a radical economic downturn or increase in our expenses could require additional financing on less than attractive rates or on terms that are excessively dilutive to existing stockholders. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. There is a risk that one or more of our current service providers, manufacturers and other partners may encounter difficulties during challenging economic times, which would directly affect our ability to attain our operating goals on schedule and on budget.

Unless our preclinical studies demonstrate the safety of our product candidates, we will not be able to commercialize our product candidates.

To obtain regulatory approval to market and sell any of our product candidates, we must satisfy the FDA and other regulatory authorities abroad, through extensive preclinical studies, that our product candidates are safe. Our *Staccato* system creates condensation aerosol from drug compounds, and there currently are no approved products that use a similar method of drug delivery. Companies developing other inhalation products have not defined or successfully completed the types of preclinical studies we believe will be required for submission to regulatory authorities as we seek approval to conduct our clinical trials. We may not conduct the types of preclinical testing eventually required by regulatory authorities, or the preclinical tests may indicate that our product candidates are not safe for use in humans. Preclinical testing is expensive, can take many years and have an uncertain outcome. In addition, success in initial preclinical testing does not ensure that later preclinical testing will be successful. We may experience numerous unforeseen events during, or as a result of, the preclinical testing process, which could delay or prevent our ability to develop or commercialize our product candidates, including:

- our preclinical testing may produce inconclusive or negative safety results, which may require us to conduct additional preclinical testing or to abandon product candidates that we believed to be promising;
- our product candidates may have unfavorable pharmacology, toxicology or carcinogenicity; and
- our product candidates may cause undesirable side effects.

Any such events would increase our costs and could delay or prevent our ability to commercialize our product candidates, which could adversely impact our business, financial condition and results of operations.

Preclinical studies indicated possible adverse impact of pulmonary delivery of AZ-001.

In our daily dosing animal toxicology studies of prochlorperazine, the active pharmaceutical ingredient, or API, in AZ-001, we detected changes to, and increases of, the cells in the upper airway of the test animals. The terms for these changes and increases are "squamous metaplasia" and "hyperplasia," respectively. We also observed lung inflammation in some animals. These findings occurred in daily dosing studies at doses that were proportionately substantially greater than any dose we expect to continue to develop or commercialize. In subsequent toxicology studies of AZ-001 involving intermittent dosing consistent with its intended use, we detected lower incidence and severity of the changes to, and increases of, the cells in the upper airway of the test animals compared to the daily dosing results. We did not observe any lung inflammation with intermittent dosing. During the second quarter of 2008, we completed a 28-day repeat dose inhalation study in dogs. Consistent with previous findings in shorter-term

and higher dose studies, we observed dose-related minimal to slight squamous metaplasia in the upper respiratory tract, primarily in the lining of the nasal passages, in all treated groups. No lower respiratory tract or lung findings were reported. These findings suggest that the delivery of the pure drug compound of AZ-001 at the proportionately higher doses used in daily dosing toxicology studies may cause adverse consequences if we were to administer prochlorperazine chronically for prolonged periods of time. If we observe these findings in our clinical trials of AZ-001, it could prevent further development or commercialization of AZ-001.

Failure or delay in commencing or completing clinical trials for our product candidates could harm our business.

To date, we have not completed all the clinical trials necessary to support an application with the FDA for approval to market any of our product candidates. Current and planned clinical trials may be delayed or terminated as a result of many factors, including:

- delays or failure in reaching agreement on acceptable clinical trial contracts or clinical trial protocols with prospective sites;
- regulators or institutional review boards may not authorize us to commence a clinical trial;
- regulators or institutional review boards may suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or concerns about patient safety;
- we may suspend or terminate our clinical trials if we believe that they expose the participating patients to unacceptable health risks;
- we may experience slower than expected patient enrollment or lack of a sufficient number of patients that meet the enrollment criteria for our clinical trials;
- patients may not complete clinical trials due to safety issues, side effects, dissatisfaction with the product candidate, or other reasons;
- we may have difficulty in maintaining contact with patients after treatment, preventing us from collecting the data required by our study protocol;
- product candidates may demonstrate a lack of efficacy during clinical trials;
- we may experience governmental or regulatory delays, failure to obtain regulatory approval or changes in regulatory requirements, policy and guidelines; and
- we may experience delays in our ability to manufacture clinical trial materials in a timely manner as a result of ongoing process and design enhancements to our *Staccato* system.

Any delay in commencing or completing clinical trials for our product candidates would delay commercialization of our product candidates and harm our business, financial condition and results of operations. It is possible that none of our product candidates will successfully complete clinical trials or receive regulatory approval, which would severely harm our business, financial condition and results of operations.

Continuing development of our single dose version device may delay regulatory submissions and marketing approval for AZ-004

Our clinical studies to date for our AZ-004, AZ-001, AZ-104, AZ-002 and AZ-007 product candidates have been completed using a version of our single dose *Staccato* device we refer to as the chemical single dose, or CSD, device. We are developing a version of the CSD which is intended to cost less to manufacture and is more scalable than the current version of CSD. We refer to the newer version of this single dose device as the commercial production device, or CPD, version. The CPD incorporates the same basic chemical heat package and electronics as the CSD. We have conducted a bioequivalence study in normal volunteers using the CSD and the CPD versions of the device to determine if the drug dose dispensed by the two devices is bioequivalent. The FDA is reviewing the results of this study. If the FDA determines that the results of the bioequivalence study and the available analytical data do not support the bioequivalency, or if the FDA or foreign regulatory authorities determine the CPD is

unacceptable for any other reason, we may be required to conduct additional clinical research for AZ-004 with the CPD version of the device. Conducting an additional Phase 3 clinical trial could delay the filing of an NDA which could also delay any potential marketing approval in the United States.

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.

Our product candidates are in preclinical and clinical development and have not received regulatory approval from the FDA or any foreign regulatory authority. The clinical development and regulatory approval process is extremely expensive and takes many years. The timing of any approval cannot be accurately predicted. If we fail to obtain regulatory approval for our current or future product candidates, we will be unable to market and sell them and therefore we may never be profitable.

As part of the regulatory process, we must conduct clinical trials for each product candidate to demonstrate safety and efficacy to the satisfaction of the FDA and other regulatory authorities abroad. The number and design of clinical trials that will be required varies depending on the product candidate, the condition being evaluated, the trial results and regulations applicable to any particular product candidate. In June 2008, we announced that on our Phase 2a proof-of-concept clinical trial of AZ-002 (*Staccato* Alprazolam) did not meet either of its two primarily endpoints.

Prior clinical trial program designs and results are not necessarily predictive of future clinical trial designs or results. Initial results may not be confirmed upon full analysis of the detailed results of a trial. Product candidates in later stage clinical trials may fail to show the desired safety and efficacy despite having progressed through initial clinical trials with acceptable endpoints.

If our product candidates fail to show a clinically significant benefit compared to placebo, they will not be approved for marketing.

Device failure rates higher than we anticipate may result in clinical trials that do not meet their specific efficacy endpoints. Device failures or improper device use by patients may impact the results of future trials. The design of our clinical trials is based on many assumptions about the expected effect of our product candidates, and if those assumptions prove incorrect, the clinical trials may not produce statistically significant results. Our *Staccato* system is not similar to other approved drug delivery methods, there is no clear precedent for the application of detailed regulatory requirements to our product candidates. We cannot assure you that the design of, or data collected from, the clinical trials of our product candidates will be sufficient to support the FDA and foreign regulatory approvals.

Regulatory authorities may not approve our product candidates even if they meet safety and efficacy endpoints in clinical trials.

The FDA and other foreign regulatory agencies can delay, limit or deny marketing approval for many reasons, including:

- a product candidate may not be considered safe or effective;
- the manufacturing processes or facilities we have selected may not meet the applicable requirements; and
- changes in their approval policies or adoption of new regulations may require additional work on our part.

Any delay in, or failure to receive or maintain, approval for any of our product candidates could prevent us from ever generating meaningful revenues or achieving profitability.

Our product candidates may not be approved even if they achieve their endpoints in clinical trials. Regulatory agencies, including the FDA, or their advisors may disagree with our trial design and our interpretations of data from preclinical studies and clinical trials. Regulatory agencies may change requirements for approval even after a clinical trial design has been approved. Regulatory agencies also may approve a product candidate for fewer or more limited indications than requested or may grant approval subject to the performance of post-marketing studies. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates.

Our product candidates will remain subject to ongoing regulatory review even if they receive marketing approval. If we fail to comply with continuing regulations, we could lose these approvals, and the sale of any future products could be suspended.

Even if we receive regulatory approval to market a particular product candidate, the FDA or a foreign regulatory authority could condition approval on conducting additional costly post-approval studies or could limit the scope of our approved labeling. Moreover, the product may later cause adverse effects that limit or prevent its widespread use, force us to withdraw it from the market or impede or delay our ability to obtain regulatory approvals in additional countries. In addition, we will continue to be subject to FDA review and periodic inspections to ensure adherence to applicable regulations. After receiving marketing approval, the FDA imposes extensive regulatory requirements on the manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion and record keeping related to the product.

If we fail to comply with the regulatory requirements of the FDA and other applicable U.S. and foreign regulatory authorities or previously unknown problems with any future products, suppliers or manufacturing processes are discovered, we could be subject to administrative or judicially imposed sanctions, including:

- restrictions on the products, suppliers or manufacturing processes;
- warning letters or untitled letters;
- civil or criminal penalties or fines;
- injunctions;
- product seizures, detentions or import bans;
- voluntary or mandatory product recalls and publicity requirements;
- suspension or withdrawal of regulatory approvals;
- total or partial suspension of production; and
- refusal to approve pending applications for marketing approval of new drugs or supplements to approved applications.

If we do not produce our devices cost effectively, we will never be profitable.

Our *Staccato* system based product candidates contain electronic and other components in addition to the active pharmaceutical ingredients. As a result of the cost of developing and producing these components, the cost to produce our product candidates, and any approved products, will likely be higher per dose than the cost to produce intravenous or oral tablet products. This increased cost of goods may prevent us from ever selling any products at a profit. In addition, we are developing single dose and multiple dose versions of our *Staccato* system. Developing multiple versions of our *Staccato* system may reduce or eliminate our ability to achieve manufacturing economies of scale. In addition, developing multiple versions of our *Staccato* system reduces our ability to focus development resources on each version, potentially reducing our ability to effectively develop any particular version. We expect to continue to modify each of our product candidates throughout their clinical development to improve their performance, dependability, manufacturability and quality. Some of these modifications may require additional regulatory review and approval, which may delay or prevent us from conducting clinical trials. The development and production of our technology entail a number of technical challenges, including achieving adequate dependability, that may be expensive or time consuming to solve. Any delay in or failure to develop and manufacture any future products in a cost effective way could prevent us from generating any meaningful revenues and prevent us from becoming profitable.

We rely on third parties to conduct our preclinical studies and our clinical trials. If these third parties do not perform as contractually required or expected, we may not be able to obtain regulatory approval for our product candidates, or we may be delayed in doing so.

We do not have the ability to conduct preclinical studies or clinical trials independently for our product candidates. We must rely on third parties, such as contract research organizations, medical institutions, academic institutions, clinical investigators and contract laboratories, to conduct our preclinical studies and clinical trials. We are responsible for confirming that our preclinical studies are conducted in accordance with applicable regulations and that each of our clinical trials is conducted in accordance with its general investigational plan and protocol. The FDA requires us to comply with regulations and standards, commonly referred to as good laboratory practices, or GLP, for conducting and recording the results of our preclinical studies and good clinical practices for conducting, monitoring, recording and reporting the results of clinical trials, to assure that data and reported results are accurate and that the clinical trial participants are adequately protected. Our reliance on third parties does not relieve us of these responsibilities. If the third parties conducting our clinical trials do not perform their contractual duties or obligations, do not meet expected deadlines, fail to comply with the FDA's good clinical practice regulations, do not adhere to our clinical trial protocols or otherwise fail to generate reliable clinical data, we may need to enter into new arrangements with alternative third parties and our clinical trials may be extended, delayed or terminated or may need to be repeated, and we may not be able to obtain regulatory approval for or commercialize the product candidate being tested in such trials.

Problems with the third parties that manufacture the active pharmaceutical ingredients in our product candidates may delay our clinical trials or subject us to liability.

We do not currently own or operate manufacturing facilities for clinical or commercial production of the API used in any of our product candidates. We have no experience in drug manufacturing, and we lack the resources and the capability to manufacture any of the APIs used in our product candidates, on either a clinical or commercial scale. As a result, we rely on third parties to supply the API used in each of our product candidates. We expect to continue to depend on third parties to supply the API for our lead product candidates and any additional product candidates we develop in the foreseeable future.

An API manufacturer must meet high precision and quality standards for that API to meet regulatory specifications and comply with regulatory requirements. A contract manufacturer is subject to ongoing periodic unannounced inspection by the FDA and corresponding state and foreign authorities to ensure strict compliance with current good manufacturing practice, or cGMP, and other applicable government regulations and corresponding foreign standards. Additionally, a contract manufacturer must pass a pre-approval inspection by the FDA to ensure strict compliance with cGMP prior to the FDA's approval of any product candidate for marketing. A contract manufacturer's failure to conform with cGMP could result in the FDA's refusal to approve or a delay in the FDA's approval of a product candidate for marketing. We are ultimately responsible for confirming that the APIs used in our product candidates are manufactured in accordance with applicable regulations.

Our third party suppliers may not carry out their contractual obligations or meet our deadlines. In addition, the API they supply to us may not meet our specifications and quality policies and procedures. If we need to find alternative suppliers of the API used in any of our product candidates, we may not be able to contract for such supplies on acceptable terms, if at all. Any such failure to supply or delay caused by such contract manufacturers would have an adverse effect on our ability to continue clinical development of our product candidates or commercialize any future products.

If our third party drug suppliers fail to achieve and maintain high manufacturing standards in compliance with cGMP regulations, we could be subject to certain product liability claims in the event such failure to comply resulted in defective products that caused injury or harm.

If we experience problems with the manufacturers of components of our product candidates, our development programs may be delayed or we may be subject to liability.

We outsource the manufacturing of some of the components of our *Staccato* system, including the printed circuit boards and the plastic airways, and we will outsource the manufacturing of the chemical heat packages to be

used in our commercial single dose device. We have no experience in the manufacturing of components (other than our current chemical heat packages), and we currently lack the resources and the capability to manufacture them, on either a clinical or commercial scale. As a result, we rely on third parties to supply these components. We expect to continue to depend on third parties to supply these components for our current product candidates and any devices based on the *Staccato* system we develop in the foreseeable future.

The third party suppliers of the components of our *Staccato* system must meet high precision and quality standards for those components to comply with regulatory requirements. A contract manufacturer is subject to ongoing periodic unannounced inspection by the FDA and corresponding state and foreign authorities to ensure strict compliance with the FDA's Quality System Regulation, or QSR, which sets forth the FDA's current good manufacturing practice requirements for medical devices and their components, and other applicable government regulations and corresponding foreign standards. We are ultimately responsible for confirming that the components used in the *Staccato* system are manufactured in accordance with the QSR or other applicable regulations.

Our third party suppliers may not comply with their contractual obligations or meet our deadlines, or the components they supply to us may not meet our specifications and quality policies and procedures. If we need to find alternative suppliers of the components used in the *Staccato* system, we may not be able to contract for such components on acceptable terms, if at all. Any such failure to supply or delay caused by such contract manufacturers would have an adverse affect on our ability to continue clinical development of our product candidates or commercialize any future products.

In addition, the heat packages used in the single dose version of our *Staccato* system are manufactured using certain energetic, or highly combustible, materials that are used to generate the rapid heating necessary for vaporizing the drug compound while avoiding degradation. Manufacture of products containing these types of materials is regulated by the U.S. government. We currently manufacture the heat packages that are being used in the devices used in our clinical trials. We have entered into a supply agreement with Autoliv for the manufacture of the heat packages in the commercial design of our single dose version of our *Staccato* system. If we are unable to manufacture the heat packages used in our ongoing clinical trials or if in the future Autoliv is unable to manufacture the heat packages to our specifications, or does not carry out its contractual obligations to supply our heat packages to us, our clinical trials may be delayed, suspended or terminated while we seek additional suitable manufacturers of our heat packages, which may prevent us from commercializing our product candidates that utilize the single dose version of the *Staccato* system.

If we do not establish additional strategic partnerships, we will have to undertake development and commercialization efforts on our own, which would be costly and delay our ability to commercialize any future products.

A key element of our business strategy is our intent to selectively partner with pharmaceutical, biotechnology and other companies to obtain assistance for the development and potential commercialization of our product candidates. In December 2006, we entered into such a development relationship with Symphony Allegro, and in December 2007 we entered into a strategic relationship with Endo Pharmaceuticals, Inc. for the development of AZ-003. In January 2009, we mutually agreed with Endo to terminate our agreement. We intend to enter into additional strategic partnerships with third parties to develop and commercialize our product candidates that are intended for larger markets, and we may enter into strategic partnerships for product candidates that are targeted toward specialty markets. To date, other than Symphony Allegro and Endo, we have not entered into any strategic partnerships for any of our product candidates. We face significant competition in seeking appropriate strategic partners, and these strategic partnerships can be intricate and time consuming to negotiate and document. We may not be able to negotiate strategic partnerships on acceptable terms, or at all. We are unable to predict when, if ever, we will enter into any additional strategic partnerships because of the numerous risks and uncertainties associated with establishing strategic partnerships. If we are unable to negotiate additional strategic partnerships for our product candidates we may be forced to curtail the development of a particular candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization, reduce the scope of our sales or marketing activities or undertake development or commercialization activities at our own expense. In addition, we will bear all the risk related to the development of that product candidate. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to

obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not have sufficient funds, we will not be able to bring our product candidates to market and generate product revenue.

If we enter into additional strategic partnerships, we may be required to relinquish important rights to and control over the development of our product candidates or otherwise be subject to terms unfavorable to us.

Due to our relationship with Symphony Allegro we are, and for any additional strategic partnerships with pharmaceutical or biotechnology companies we will be, subject to a number of risks, including:

- we may not be able to control the amount and timing of resources that our strategic partners devote to the development or commercialization of product candidates;
- strategic partners may delay clinical trials, provide insufficient funding, terminate a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new version of a product candidate for clinical testing;
- strategic partners may not pursue further development and commercialization of products resulting from the strategic partnering arrangement or may elect to discontinue research and development programs;
- strategic partners may not commit adequate resources to the marketing and distribution of any future products, limiting our potential revenues from these products;
- disputes may arise between us and our strategic partners that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management's attention and consumes resources;
- strategic partners may experience financial difficulties;
- strategic partners may not properly maintain or defend our intellectual property rights or may use our proprietary information in a manner that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- business combinations or significant changes in a strategic partner's business strategy may also adversely affect a strategic partner's willingness or ability to complete its obligations under any arrangement;
- strategic partners could independently move forward with a competing product candidate developed either independently or in collaboration with others, including our competitors; and
- strategic partners could terminate the arrangement or allow it to expire, which would delay the development and may increase the cost of developing our product candidates.

We have exclusively licensed certain intellectual property rights to Staccato alprazolam and Staccato loxapine in connection with our Symphony Allegro arrangement and will not receive material future royalties or revenues with respect to this intellectual property unless we exercise an option to repurchase the rights to the programs in the future through the acquisition of Symphony Allegro. We may not obtain sufficient clinical data in order to determine whether we should exercise this option prior to the expiration of the development period, and even if we decide to exercise the option, we may not have the financial resources to exercise it in a timely manner.

In December 2006, we entered into a transaction involving a series of related agreements providing for the financing of additional clinical and nonclinical development of *Staccato* alprazolam, our AZ-002 program, and *Staccato* loxapine, our AZ-004 and AZ-104 programs. Pursuant to the agreements, Symphony Capital LLC and its investors have invested $50 million to form Symphony Allegro, to fund additional clinical and nonclinical development of *Staccato* alprazolam and *Staccato* loxapine. We have exclusively licensed to Symphony Allegro certain intellectual property rights related to *Staccato* alprazolam and *Staccato* loxapine. We have retained manufacturing rights to these product candidates. As part of the arrangement, we received an option granting us the exclusive right, but not the obligation, to acquire the licensed programs at specified points in time at specified prices during the term of the development period through the acquisition of Symphony Allegro. The development

programs under the arrangement are jointly managed by Symphony Allegro and us, and there can be no assurance that we will agree on various decisions that will enable us to successfully develop the potential products, or even if we are in agreement on the development plans, that the development efforts will result in sufficient clinical data to make a fully informed decision with respect to the exercise of our option. If we do not exercise our purchase option by December 1, 2010, then Symphony Allegro will retain its exclusive license to develop and commercialize *Staccato* alprazolam and *Staccato* loxapine for all indications, and we will maintain exclusive rights to manufacture and sell *Staccato* alprazolam and *Staccato* loxapine to Symphony Allegro or its sublicensee for those purposes.

If we elect to exercise the purchase option, we will be required to make a payment estimated to be between $92.5 million at March 31, 2009 and $122.5 million at December 1, 2010, which at our election may be paid partially in shares of our common stock. As a result, in order to exercise the option, we will be required to make a substantial payment of cash and possibly issue a substantial number of shares of our common stock. We do not currently have the resources to exercise the option, and we may be required to enter into a financing arrangement or license arrangement with one or more third parties, or some combination of these, in order to exercise the option, even if we paid a portion of the purchase price with our common stock. There can be no assurance that any financing or licensing arrangement will be available or even if available, that the terms would be favorable to us and our stockholders. In addition, the exercise of the purchase option may require us to record a significant charge to earnings and may adversely impact future operating results.

If we fail to gain market acceptance among physicians, patients, third-party payors and the medical community, we will not become profitable.

The *Staccato* system is a fundamentally new method of drug delivery. Any future product based on our *Staccato* system may not gain market acceptance among physicians, patients, third-party payors and the medical community. If these products do not achieve an adequate level of acceptance, we will not generate sufficient product revenues to become profitable. The degree of market acceptance of any of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- demonstration of efficacy and safety in clinical trials;
- the existence, prevalence and severity of any side effects;
- potential or perceived advantages or disadvantages compared to alternative treatments;
- perceptions about the relationship or similarity between our product candidates and the parent drug compound upon which each product candidate is based;
- the timing of market entry relative to competitive treatments;
- the ability to offer any future products for sale at competitive prices;
- relative convenience, product dependability and ease of administration;
- the strength of marketing and distribution support;
- the sufficiency of coverage and reimbursement of our product candidates by governmental and other third-party payors; and
- the product labeling or product insert required by the FDA or regulatory authorities in other countries.

Our pipeline may be limited by the number of drug compounds suitable for use with the Staccato system.

The current versions of the *Staccato* system cannot deliver large molecule drugs, such as peptides and proteins. In addition, the physical size of the metal substrates in the single dose and multiple dose versions of the *Staccato* system limits their use to drugs that require dose amounts less than 10 to 15 milligrams and 100 to 200 micrograms, respectively. Further, approximately 200 of the 400 small molecule compounds we have screened for initial vaporization feasibility did not form drug aerosols with the 97% purity we use as an internal standard for further development. There are also many drug compounds that are covered by composition of matter patents that prevent us from developing the compound in the *Staccato* system without a license from the patent owner, which may not be

available on acceptable terms, if at all. If we are not able to identify additional drug compounds that can be developed with the *Staccato* system, we may not develop enough products to develop a sustainable business.

AZ-001 and other product candidates that we may develop may require expensive carcinogenicity tests.

The API in AZ-001, prochlorperazine, was approved by the FDA in 1956 for the treatment of severe nausea and vomiting. At that time, the FDA did not require the carcinogenicity testing that is now generally required for marketing approval. It is unclear whether we will be required to perform such testing prior to filing our application for marketing approval of AZ-001 or whether we will be allowed to perform such testing after we file an application. Such carcinogenicity testing will be expensive and require significant additional resources to complete and may delay approval to market AZ-001. We may encounter similar requirements with other product candidates incorporating drugs that have not undergone carcinogenicity testing. Any carcinogenicity testing we are required to complete will increase the costs to develop a particular product candidate and may delay or halt the development of such product candidate.

If some or all of our patents expire, are invalidated or are unenforceable, or if some or all of our patent applications do not yield issued patents or yield patents with narrow claims, competitors may develop competing products using our or similar intellectual property and our business will suffer.

Our success will depend in part on our ability to obtain and maintain patent and trade secret protection for our technologies and product candidates both in the United States and other countries. We do not know whether any patents will issue from any of our pending or future patent applications. In addition, a third party may successfully circumvent our patents. Our rights under any issued patents may not provide us with sufficient protection against competitive products or otherwise cover commercially valuable products or processes.

The degree of protection for our proprietary technologies and product candidates is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- we might not have been the first to make the inventions covered by each of our pending patent applications and issued patents;
- we might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- it is possible that none of our pending patent applications will result in issued patents;
- the claims of our issued patents may be narrower than as filed and not sufficiently broad to prevent third parties from circumventing them;
- we may not develop additional proprietary technologies or drug candidates that are patentable;
- our patent applications or patents may be subject to interference, opposition or similar administrative proceedings;
- any patents issued to us or our potential strategic partners may not provide a basis for commercially viable products or may be challenged by third parties in the course of litigation or administrative proceedings such as reexaminations or interferences; and
- the patents of others may have an adverse effect on our ability to do business.

Even if valid and enforceable patents cover our product candidates and technologies, the patents will provide protection only for a limited amount of time.

Our and our potential strategic partners' ability to obtain patents is uncertain because, to date, some legal principles remain unresolved, there has not been a consistent policy regarding the breadth or interpretation of claims allowed in patents in the United States, and the specific content of patents and patent applications that are necessary to support and interpret patent claims is highly uncertain due to the complex nature of the relevant legal, scientific

and factual issues. Furthermore, the policies governing pharmaceutical and medical device patents outside the United States may be even more uncertain. Changes in either patent laws or interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property or narrow the scope of our patent protection.

Even if patents are issued regarding our product candidates or methods of using them, those patents can be challenged by our competitors who can argue that our patents are invalid and/or unenforceable. Third parties may challenge our rights to, or the scope or validity of, our patents. Patents also may not protect our product candidates if competitors devise ways of making these or similar product candidates without legally infringing our patents. The Federal Food, Drug and Cosmetic Act and the FDA regulations and policies provide incentives to manufacturers to challenge patent validity or create modified, non-infringing versions of a drug or device in order to facilitate the approval of generic substitutes. These same types of incentives encourage manufacturers to submit new drug applications that rely on literature and clinical data not prepared for or by the drug sponsor.

We also rely on trade secrets to protect our technology, especially where we do not believe that patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. The employees, consultants, contractors, outside scientific collaborators and other advisors of our company and our strategic partners may unintentionally or willfully disclose our confidential information to competitors. Enforcing a claim that a third party illegally obtained and is using our trade secrets is expensive and time consuming and the outcome is unpredictable. Failure to protect or maintain trade secret protection could adversely affect our competitive business position.

Our research and development collaborators may have rights to publish data and other information in which we have rights. In addition, we sometimes engage individuals or entities to conduct research that may be relevant to our business. The ability of these individuals or entities to publish or otherwise publicly disclose data and other information generated during the course of their research is subject to certain contractual limitations. These contractual provisions may be insufficient or inadequate to protect our trade secrets and may impair our patent rights. If we do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our technology and other confidential information, then our ability to receive patent protection or protect our proprietary information may be jeopardized.

Litigation or other proceedings or third party claims of intellectual property infringement could require us to spend time and money and could shut down some of our operations.

Our commercial success depends in part on not infringing patents and proprietary rights of third parties. Others have filed, and in the future are likely to file, patent applications covering products that are similar to our product candidates, as well as methods of making or using similar or identical products. If these patent applications result in issued patents and we wish to use the claimed technology, we would need to obtain a license from the third party. We may not be able to obtain these licenses at a reasonable cost, if at all.

In addition, administrative proceedings, such as interferences and reexaminations before the U.S. Patent and Trademark Office, could limit the scope of our patent rights. We may incur substantial costs and diversion of management and technical personnel as a result of our involvement in such proceedings. In particular, our patents and patent applications may be subject to interferences in which the priority of invention may be awarded to a third party. We do not know whether our patents and patent applications would be entitled to priority over patents or patent applications held by such a third party. Our issued patents may also be subject to reexamination proceedings. We do not know whether our patents would survive reexamination in light of new questions of patentability that may be raised following their issuance.

Third parties may assert that we are employing their proprietary technology or their proprietary products without authorization. In addition, third parties may already have or may obtain patents in the future and claim that use of our technologies or our products infringes these patents. We could incur substantial costs and diversion of management and technical personnel in defending our self against any of these claims. Furthermore, parties making claims against us may be able to obtain injunctive or other equitable relief, which could effectively block our ability to further develop, commercialize and sell any future products and could result in the award of substantial damages against us. In the event of a successful claim of infringement against us, we may be required to pay damages and obtain one or more licenses from third parties. We may not be able to obtain these licenses at a reasonable cost, if at

all. In that event, we could encounter delays in product introductions while we attempt to develop alternative methods or products. In the event we cannot develop alternative methods or products, we may be effectively blocked from developing, commercializing or selling any future products. Defense of any lawsuit or failure to obtain any of these licenses would be expensive and could prevent us from commercializing any future products.

We review from time to time publicly available information concerning the technological development efforts of other companies in our industry. If we determine that these efforts violate our intellectual property or other rights, we intend to take appropriate action, which could include litigation. Any action we take could result in substantial costs and diversion of management and technical personnel in enforcing our patents or other intellectual property rights against others. Furthermore, the outcome of any action we take to protect our rights may not be resolved in our favor.

Competition in the pharmaceutical industry is intense. If our competitors are able to develop and market products that are more effective, safer or less costly than any future products that we may develop, our commercial opportunity will be reduced or eliminated.

We face competition from established as well as emerging pharmaceutical and biotechnology companies, as well as from academic institutions, government agencies and private and public research institutions. Our commercial opportunity will be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer side effects or are less expensive than any future products that we may develop and commercialize. In addition, significant delays in the development of our product candidates could allow our competitors to bring products to market before us and impair our ability to commercialize our product candidates.

We anticipate that, if approved, AZ-004 would compete with the available intramuscular, or IM, injectable form and oral forms of loxapine and other forms of available antipsychotic drugs for the treatment of agitation.

We anticipate that, if approved, AZ-001 and AZ-104 would compete with currently marketed triptan drugs and with other migraine headache treatments, including intravenous, or IV, delivery of prochlorperazine, the API in AZ-001. In addition, we are aware of at least 15 product candidates in development for the treatment of migraines, including triptan products.

We anticipate that, if approved, AZ-003 would compete with some of the available forms of fentanyl, including injectable fentanyl, oral transmucosal fentanyl formulations and ionophoretic transdermal delivery of fentanyl. We are also aware of three fentanyl products under review by regulatory agencies either in the United States or abroad, and at least 19 products in Phase 3 clinical trial development for acute pain, seven of which are fentanyl products. There are two inhaled forms of fentanyl products that are in Phase 2 development. In addition, if approved, AZ-003 would compete with various generic opioid drugs, such as oxycodone, hydrocodone and morphine, or combination products including one or more of such drugs.

We anticipate that, if approved, AZ-007 would compete with non-benzodiazepine GABA-A receptor agonists, which include Ambien® (immediate release and controlled-release tablets), Sonata®, and Lunesta®. We are also aware of more than 10 generic versions of zolpidem (brand Ambien) oral tablets and one zaleplon (brand Sonata) that have been tentatively approved by the FDA, as well as at least five insomnia products that are under review by the FDA. Additionally, we are aware of three products in Phase 3 development for the treatment of insomnia.

We anticipate that, if approved, AZ-002 would compete with the oral tablet form of alprazolam and possibly intravenous and oral forms of other benzodiazepines.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Established pharmaceutical companies may invest heavily to discover quickly and develop novel compounds or drug delivery technology that could make our product candidates obsolete. Smaller or early stage companies may also prove to be significant competitors, particularly through strategic partnerships with large and established companies. In addition, these third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies and technology licenses complementary to our

programs or advantageous to our business. Accordingly, our competitors may succeed in obtaining patent protection, receiving FDA approval or discovering, developing and commercializing products before we do. If we are not able to compete effectively against our current and future competitors, our business will not grow and our financial condition will suffer.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate significant product revenue.

We have conducted a comprehensive strategic marketing review and developed our initial launch strategy for our lead product candidate, AZ-004. We do not have a sales organization and have no experience in the sales and distribution of pharmaceutical products. There are risks involved with establishing our own sales capabilities and increasing our marketing capabilities, as well as entering into arrangements with third parties to perform these services. Developing an internal sales force is expensive and time consuming and could delay any product launch. On the other hand, if we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues are likely to be lower than if we market and sell any products that we develop ourselves.

We may establish our own specialty sales force and/or engage pharmaceutical or other healthcare companies with an existing sales and marketing organization and distribution systems to sell, market and distribute any future products. We may not be able to establish a specialty sales force or establish sales and distribution relationships on acceptable terms. Factors that may inhibit our efforts to commercialize any future products without strategic partners or licensees include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to or persuade adequate numbers of physicians to prescribe any future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

Because the establishment of sales and marketing capabilities depends on the progress towards commercialization of our product candidates and because of the numerous risks and uncertainties involved with establishing our own sales and marketing capabilities, we are unable to predict when, if ever, we will establish our own sales and marketing capabilities. However, we do not anticipate establishing sales capabilities until at least 2010. If we are not able to partner with a third party and are unsuccessful in recruiting sales and marketing personnel or in building a sales and marketing infrastructure, we will have difficulty commercializing our product candidates, which would adversely affect our business and financial condition.

If we lose our key personnel or are unable to attract and retain additional personnel, we may be unable to develop or commercialize our product candidates.

We are highly dependent on our President and Chief Executive Officer, Thomas B. King, the loss of whose services might adversely impact the achievement of our objectives. In addition, recruiting and retaining qualified clinical, scientific and engineering personnel to manage clinical trials of our product candidates and to perform future research and development work will be critical to our success. There is currently a shortage of skilled executives in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. Although we believe we will be successful in attracting and retaining qualified personnel, competition for experienced management and clinical, scientific and engineering personnel from numerous companies and academic and other research institutions may limit our ability to do so on acceptable terms. In addition, we do not have employment agreements with any of our employees, and they could leave our employment at will. We have change of control agreements with our executive officers and vice presidents that provide for certain benefits upon termination or a change in role or responsibility in connection with a change of control of our company. We do not maintain life insurance policies on any employees. Failure to attract and retain personnel would prevent us from developing and commercializing our product candidates.

If plaintiffs bring product liability lawsuits against us, we may incur substantial liabilities and may be required to limit commercialization of the product candidates that we may develop.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates in clinical trials and will face an even greater risk if we commercialize any products. We may be held liable if any product we develop causes injury or is found otherwise unsuitable during product testing, manufacturing, marketing or sale. Regardless of merit or eventual outcome, liability claims may result in decreased demand for any product candidates or products that we may develop, injury to our reputation, withdrawal of clinical trials, costs to defend litigation, substantial monetary awards to clinical trial participants or patients, loss of revenue and the inability to commercialize any products that we develop. We have product liability insurance that covers our clinical trials up to a $10 million aggregate annual limit. We intend to expand product liability insurance coverage to include the sale of commercial products if we obtain marketing approval for any products that we may develop. However, this insurance may be prohibitively expensive, or may not fully cover our potential liabilities. Inability to obtain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims could prevent or delay the commercialization of our product candidates. If we are sued for any injury caused by any future products, our liability could exceed our total assets.

Our product candidates AZ-002, AZ-003 and AZ-007 contain drug substances which are regulated by the U.S. Drug Enforcement Administration. Failure to comply with applicable regulations could harm our business.

The Controlled Substances Act imposes various registration, recordkeeping and reporting requirements, procurement and manufacturing quotas, labeling and packaging requirements, security controls and a restriction on prescription refills on certain pharmaceutical products. A principal factor in determining the particular requirements, if any, applicable to a product is its actual or potential abuse profile. The U.S. Drug Enforcement Administration, or DEA, regulates chemical compounds as Schedule I, II, III, IV or V substances, with Schedule I substances considered to present the highest risk of substance abuse and Schedule V substances the lowest risk. Alprazolam, the API in AZ-002, is regulated as a Schedule IV substance, fentanyl, the API in AZ-003, is regulated as a Schedule II substance, and zaleplon, the API in AZ-007, is regulated as a Schedule IV substance. Each of these product candidates is subject to DEA regulations relating to manufacture, storage, distribution and physician prescription procedures, and the DEA regulates the amount of the scheduled substance that would be available for clinical trials and commercial distribution. As a Schedule II substance, fentanyl is subject to more stringent controls, including quotas on the amount of product that can be manufactured as well as a prohibition on the refilling of prescriptions without a new prescription from the physician. The DEA periodically inspects facilities for compliance with its rules and regulations. Failure to comply with current and future regulations of the DEA could lead to a variety of sanctions, including revocation, or denial of renewal, or of DEA registrations, injunctions, or civil or criminal penalties and could harm our business, financial condition and results of operations.

The single dose version of our Staccato system contains materials that are regulated by the U.S. government, and failure to comply with applicable regulations could harm our business.

The single dose version of our *Staccato* system uses energetic materials to generate the rapid heating necessary for vaporizing the drug, while avoiding degradation. Manufacture of products containing energetic materials is controlled by the U.S. Bureau of Alcohol, Tobacco, Firearms and Explosives, or ATF. Technically, the energetic materials used in our *Staccato* system are classified as "low explosives," and the ATF has granted us a license/permit for the manufacture of such low explosives. Additionally, due to inclusion of the energetic materials in our *Staccato* system, the Department of Transportation, or DOT, regulates shipments of the single dose version of our *Staccato* system. The DOT has granted the single dose version of our *Staccato* system "Not Regulated as an Explosive" status. Failure to comply with the current and future regulations of the ATF or DOT could subject us to future liabilities and could harm our business, financial condition and results of operations. Furthermore, these regulations could restrict our ability to expand our facilities or construct new facilities or could require us to incur other significant expenses in order to maintain compliance.

We use hazardous chemicals and highly combustible materials in our business. Any claims relating to improper handling, storage or disposal of these materials could be time consuming and costly.

Our research and development processes involve the controlled use of hazardous materials, including chemicals. We also use energetic materials in the manufacture of the chemical heat packages that are used in our single dose devices. Our operations produce hazardous waste products. We cannot eliminate the risk of accidental contamination or discharge or injury from these materials. Federal, state and local laws and regulations govern the use, manufacture, storage, handling and disposal of these materials. We could be subject to civil damages in the event of an improper or unauthorized release of, or exposure of individuals to, hazardous materials. In addition, claimants may sue us for injury or contamination that results from our use or the use by third parties of these materials and our liability may exceed our total assets. We maintain insurance for the use of hazardous materials in the aggregate amount of $1 million, which may not be adequate to cover any claims. Compliance with environmental and other laws and regulations may be expensive, and current or future regulations may impair our research, development or production efforts.

Certain of our suppliers are working with these types of hazardous and highly combustible materials in connection with our component manufacturing agreements. In the event of a lawsuit or investigation, we could be held responsible for any injury caused to persons or property by exposure to, or release of, these hazardous and highly combustible materials. Further, under certain circumstances, we have agreed to indemnify our suppliers against damages and other liabilities arising out of development activities or products produced in connection with these agreements.

We will need to implement additional finance and accounting systems, procedures and controls in the future as we grow and to satisfy new reporting requirements.

The laws and regulations affecting public companies, including the provisions of the Sarbanes-Oxley Act of 2002, or Sarbanes-Oxley, and rules enacted and proposed by the SEC and by the Nasdaq Global Market, will result in increased costs to us as we continue to undertake efforts to comply with rules and respond to the requirements applicable to public companies. The rules make it more difficult and costly for us to obtain certain types of insurance, including director and officer liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage as compared to the polices previously available to public companies. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or our board committees or as executive officers.

As a public company, we need to comply with Sarbanes-Oxley and the related rules and regulations of the SEC, including expanded disclosure, accelerated reporting requirements and more complex accounting rules. Compliance with Section 404 of Sarbanes-Oxley and other requirements will continue to increase our costs and require additional management resources. We have been upgrading our finance and accounting systems, procedures and controls and will need to continue to implement additional finance and accounting systems, procedures and controls as we grow to satisfy new reporting requirements. We currently do not have an internal audit group. In addition, we may need to hire additional legal and accounting staff with appropriate experience and technical knowledge, and we cannot assure you that if additional staffing is necessary that we will be able to do so in a timely fashion.

Our facilities are located near known earthquake fault zones, and the occurrence of an earthquake or other catastrophic disaster could damage our facilities and equipment, which could cause us to curtail or cease operations.

Our facilities are located in the San Francisco Bay Area near known earthquake fault zones and, therefore, are vulnerable to damage from earthquakes. We are also vulnerable to damage from other types of disasters, such as power loss, fire, floods and similar events. If any disaster were to occur, our ability to operate our business could be seriously impaired. We currently may not have adequate insurance to cover our losses resulting from disasters or other similar significant business interruptions, and we do not plan to purchase additional insurance to cover such losses due to the cost of obtaining such coverage. Any significant losses that are not recoverable under our insurance policies could seriously impair our business, financial condition and results of operations.

Risks Relating to Owning Our Common Stock

Our stock price has been and may continue to be extremely volatile.

Our common stock price has experienced large fluctuations since our initial public offering in March 2006. In addition, the trading prices of life science and biotechnology company stocks in general have experienced extreme price fluctuations in recent years. The valuations of many life science companies without consistent product revenues and earnings are extraordinarily high based on conventional valuation standards, such as price to revenue ratios. These trading prices and valuations may not be sustained. Any negative change in the public's perception of the prospects of life science or biotechnology companies could depress our stock price regardless of our results of operations. Other broad market and industry factors may decrease the trading price of our common stock, regardless of our performance. Market fluctuations, as well as general political and economic conditions such as terrorism, military conflict, recession or interest rate or currency rate fluctuations, also may decrease the trading price of our common stock. In addition, our stock price could be subject to wide fluctuations in response to various factors, including:

- actual or anticipated results and timing of our clinical trials;
- actual or anticipated regulatory approvals of our product candidates or competing products;
- changes in laws or regulations applicable to our product candidates;
- changes in the expected or actual timing of our development programs, including delays or cancellations of clinical trials for our product candidates;
- period to period fluctuations in our operating results;
- announcements of new technological innovations or new products by us or our competitors;
- changes in financial estimates or recommendations by securities analysts;
- conditions or trends in the life science and biotechnology industries;
- changes in the market valuations of other life science or biotechnology companies;
- developments in domestic and international governmental policy or regulations;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;
- additions or departures of key personnel;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- sales of our common stock (or other securities) by us, including sales under our equity line of credit arrangement with Azimuth; and
- sales and distributions of our common stock by our stockholders.

In the past, stockholders have often instituted securities class action litigation after periods of volatility in the market price of a company's securities. If a stockholder files a securities class action suit against us, we would incur substantial legal fees, and our management's attention and resources would be diverted from operating our business in order to respond to the litigation.

If we sell shares of our common stock under our equity line of credit or in other future financings, existing common stock holders will experience immediate dilution and, as a result, our stock price may go down.

We will need to raise additional capital to fund our operations, to develop our product candidates, to develop our manufacturing capabilities and to repurchase rights from Symphony Allegro. We may obtain such financing through the sale of our equity securities from time to time. As a result, our existing common stockholders will

experience immediate dilution upon any such issuance. For example, in March 2008, we entered into a common stock purchase agreement with Azimuth, or the purchase agreement, which provides that, upon the terms and subject to the conditions set forth in the purchase agreement, Azimuth is committed to purchase up to $50 million of our common stock at times and in amounts determined by us. Our existing common stockholders will experience immediate dilution upon the purchase of any shares of our common stock by Azimuth pursuant to the purchase agreement.

Item 1B. ***Unresolved Staff Comments***

None.

Item 2. ***Properties***

We lease two buildings with an aggregate of 106,894 square feet of manufacturing, office, and laboratory facilities in Mountain View, California, which we began to occupy in the fourth quarter of 2007. We currently occupy 87,560 square feet of these facilities and sublease the remaining 19,334 square feet. The lease for both facilities expires on March 31, 2018, and we have two options to extend the lease for five years each. Our sublease agreement expires on April 30, 2009. We believe that the Mountain View facilities are sufficient for our office, manufacturing and laboratory needs for at least the next three years.

Item 3. ***Legal Proceedings***

None

Item 4. ***Submission of Matters to a Vote of Security Holders***

None.

PART II

Item 5. ***Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities***

Our common stock trades on the NASDAQ Global Market under the symbol "ALXA." The following table sets forth, for the periods indicated, the high and low sales prices of our common stock.

2008	High	Low
First Quarter	$8.16	$5.76
Second Quarter	7.55	3.75
Third Quarter	6.20	3.85
Fourth Quarter	4.91	1.16
2007	**High**	**Low**
First Quarter	$15.80	$8.52
Second Quarter	12.80	7.86
Third Quarter	10.10	7.11
Fourth Quarter	9.72	7.00

As of December 31, 2008, there were 171 holders of record of our common stock. We have not paid cash dividends on our common stock since our inception, and we do not anticipate paying any in the foreseeable future.

Item 5B. ***Use of Proceeds from the Sale of Registered Securities***

None

Item 5C. ***Treasury Stock***

None

Item 6. *Selected Financial Data*

The data set forth below should be read in conjunction with Management's Discussion and Analysis of Financial Condition and Results of Operations and the consolidated financial statements and related notes included elsewhere herein.

	Year Ended December 31,					Period from December 19, 2000 (Inception) to December 31, 2008
	2008	2007	2006	2005	2004	
	(In thousands, except per share data)					
Consolidated Statement of Operations Data:						
Revenue	$ 486	$ —	$ 1,028	$ 2,230	$ 2,436	$ 7,431
Operating expenses:						
Research and development(1)	61,565	45,645	36,494	26,235	15,147	204,683
General and administrative(1)	17,641	14,888	9,969	9,654	4,155	62,704
Acquired in-process research and development	—	—	—	—	—	3,916
Total operating expenses(1)	79,206	60,533	46,463	35,889	19,302	271,303
Loss from operations	(78,720)	(60,533)	(45,435)	(33,659)	(16,866)	(263,872)
Interest and other income and interest expense, net	1,679	4,623	1,909	1,257	241	10,225
Loss before noncontrolling interest in Symphony Allegro, Inc.	(77,041)	(55,910)	(43,526)	(32,402)	(16,625)	(253,647)
Loss attributed to noncontrolling interest in Symphony Allegro, Inc.	18,591	10,791	1,720	—	—	31,102
Net loss	$(58,450)	$(45,119)	$(41,806)	$(32,402)	$(16,625)	$(222,545)
Basic and diluted net loss per common share	$ (1.81)	$ (1.58)	$ (2.13)	$ (18.98)	$ (11.41)	
Shares used to compute basic and diluted net loss per common share	32,297	28,605	19,584	1,707	1,457	

(1) Includes stock-based compensation as follows:

	Year Ended December 31,					Period from December 19, 2000 (Inception) to December 31, 2008
	2008	2007	2006	2005	2004	
	(In thousands)					
Research and development	$2,926	$1,885	$1,770	$ 167	$59	$ 6,852
General and administrative	2,520	1,531	447	874	—	5,372
Total	$5,446	$3,416	$2,217	$1,041	$59	$12,224

During the year ended December 31, 2005, we recorded compensation expense in relation to the extinguishment of officer notes receivable, representing $875,000 of research and development expense and $3.1 million of general and administrative expense.

	December 31,				
	2008	2007	2006	2005	2004
			(In thousands)		
Consolidated Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 37,556	$ 69,391	$ 42,623	$ 38,369	$ 62,294
Investments held by Symphony Allegro, Inc.	21,318	39,449	49,956	—	—
Working capital	42,771	106,092	79,649	30,760	60,027
Total assets	84,635	149,125	105,766	47,405	69,280
Noncurrent portion of equipment financing obligations	2,515	6,317	5,865	5,155	1,840
Convertible preferred stock	—	—	—	107,194	107,194
Deficit accumulated during development stage	(222,545)	(164,095)	(118,976)	(77,170)	(44,768)
Total stockholders' equity (deficit)	33,693	75,991	49,774	(74,385)	(43,396)

Item 7. *Management's Discussion and Analysis of Financial Condition and Results of Operations*

The following Management's Discussion and Analysis of Financial Condition and Results of Operations contains forward-looking statements that are based upon current expectations. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "expect," "plan," "anticipate," "believe," "estimate," "predict," "intend," "potential" or "continue" or the negative of these terms or other comparable terminology. Forward-looking statements involve risks and uncertainties. Our actual results and the timing of events could differ materially from those discussed in our forward-looking statements as a result of many factors, including those set forth under "Risk Factors" and elsewhere in this Annual Report on Form 10-K.

Overview

We are a pharmaceutical development company focused on the research, development, and commercialization of novel proprietary products for the acute treatment of central nervous system, or CNS, conditions. All of our product candidates are based on our proprietary technology, the *Staccato* system. The *Staccato* system, vaporizes an excipient-free drug to form a condensation aerosol that, when inhaled, allows for rapid systemic drug delivery. Because of the particle size of the aerosol, the drug is quickly absorbed through the deep lung into the bloodstream, providing speed of therapeutic onset that is comparable to intravenous, or IV, administration but with greater ease, patient comfort and convenience. We currently have six product candidates in various stages of clinical development, ranging from Phase 1 through late-stage Phase 3. In 2009, our focus will be on the continued rapid development of AZ-004.

We have identified approximately 200 drug compounds that have demonstrated initial vaporization feasibility for delivery with our technology. We believe that a number of these drug compounds, when delivered by the *Staccato* system, will have a desirable therapeutic profile for the treatment of acute and intermittent conditions. We are initially focusing on developing proprietary products by combining our *Staccato* system with small molecule drugs that have been in use for many years and are well characterized to create aerosolized forms of these drugs. We believe that we will be able to reduce the development time and risks associated with our product candidates, compared to the development of new chemical entities.

Our clinical-stage product candidates are:

- *AZ-004 (Staccato loxapine).* We are developing AZ-004 for the acute treatment of agitation in patients with schizophrenia or bipolar disorder. In 2008 we successfully completed two pivotal Phase 3 clinical trials and we project a New Drug Application, or NDA, submission in the first quarter of 2010.
- *AZ-104 (Staccato loxapine).* We are developing AZ-104 to treat patients suffering from acute migraine headaches. AZ-104 is a lower-dose version of AZ-004. AZ-104 has completed a Phase 2a in-clinic study and we initiated an out-patient Phase 2b clinical trial in January 2009. AZ-104 has been licensed to Symphony Allegro, and we have the right to repurchase all rights to this product candidate

- *AZ-001 (Staccato prochlorperazine).* We are developing AZ-001 to treat patients suffering from acute migraine headaches. During the third quarter of 2008, we conducted an end-of-Phase 2 meeting with the FDA. We believe we have a clear understanding of the development requirements for filing an NDA for this product candidate. We do not intend to conduct any AZ-001 Phase 3 studies without a partner, and we are continuing to seek partners for our *Staccato* migraine product candidates, AZ-001 and AZ-104.

- *AZ-007 (Staccato zaleplon).* We are developing AZ-007 for the treatment of insomnia in patients who have difficulty falling asleep, including patients who awake in the middle of the night and have difficulty falling back asleep. AZ-007 has completed Phase 1 testing. We do not intend to conduct any AZ-007 Phase 2 studies without a partner in 2009.

- *AZ-003 (Staccato fentanyl).* We are developing AZ-003 for the treatment of patients with acute pain, including patients with breakthrough cancer pain and postoperative patients with acute pain episodes. We have completed and announced positive results from a Phase 1 clinical trial of AZ-003 in opioid naïve healthy subjects.

  In December 2007, we entered into a license, development and supply agreement, or the license agreement, with Endo Pharmaceuticals, Inc., or Endo, for AZ-003 and the fentanyl class of molecules for North America. Under the terms of the license agreement, Endo paid us an upfront fee of $10 million, and was obligated to pay potential additional milestone payments of up to $40 million upon achievement of predetermined regulatory and clinical milestones. Endo was also obligated to pay undisclosed royalties to us on net sales of the product, from which we would be required to pay for the cost of goods for the manufacture of the commercial version of the product. Under the terms of the license agreement, we had the primary responsibility for the development and costs of the *Staccato* Electronic Multiple Dose device and the exclusive right to manufacture the product for clinical development and commercial supply. Endo had the responsibility for future pre-clinical, clinical and regulatory development, and, if AZ-003 was approved for marketing, for commercializing the product in North America. In January 2009, we mutually agreed with Endo to terminate the license agreement, With all rights to AZ-003 reverting back to us. We recorded the $10 million upfront fee we received from Endo in January 2008 as deferred revenue and began to recognize this revenue in the third quarter of 2008 over the estimated performance period of six years, resulting in revenue of $486,000 in 2008. Our obligations under the license agreement were fulfilled upon the termination of the agreement, and we will recognize the remaining deferred revenue in the first quarter of 2009. We do not expect to pursue the development of AZ-003 without a partner.

- *AZ-002 (Staccato alprazolam).* AZ-002 has completed a Phase 2a proof-of-concept clinical trial for the treatment of panic attacks, an indication the Company is not planning to pursue. However, given the safety profile, the successful and reproducible delivery of alprazolam, and the IV-like pharmacological effect demonstrated to date, we and Symphony Allegro are assessing AZ-002 for other possible indications and renewed clinical development. AZ-002 has been licensed to Symphony Allegro, and we have the right to repurchase all rights to this product candidate.

In December 2006, we entered into a transaction involving a series of related agreements providing for the financing of additional clinical and nonclinical development of AZ-002, *Staccato* alprazolam, and AZ-004/AZ-104, *Staccato* loxapine. Pursuant to the agreements, Symphony Capital LLC, a wholly owned subsidiary of Symphony Holdings LLC, and its investors have invested $50 million to form Symphony Allegro to fund additional clinical and nonclinical development of *Staccato* alprazolam and *Staccato* loxapine. We have exclusively licensed to Symphony Allegro certain intellectual property rights related to *Staccato* alprazolam and *Staccato* loxapine. We have retained manufacturing rights to these product candidates. We continue to be primarily responsible for the development of these product candidates in accordance with a development plan and related development budgets, and we have incurred and may continue to incur expenses that are not funded by Symphony Allegro. Pursuant to the agreements, we have received an exclusive purchase option that gives us the right, but not the obligation, to acquire all, but not less than all, of the equity of Symphony Allegro, and reacquire the intellectual property rights that we licensed to Symphony Allegro. This purchase option is exercisable at predetermined prices between $92.5 million at March 31, 2009 and $122.5 million at December 1, 2010. The purchase option exercise price may be paid for in cash or in a combination of cash and our common stock, in our sole discretion, provided that the common stock portion may not

exceed 40% of the purchase option exercise price or 10% of our common stock issued and outstanding as of the purchase option closing date. If we pay a portion of the purchase option exercise price in shares of our common stock, then we will be required to register such shares for resale under a resale registration statement pursuant to the terms of a registration rights agreement. If we do not exercise our purchase option by December 1, 2010, then Symphony Allegro will retain its exclusive license to develop and commercialize *Staccato* alprazolam and *Staccato* loxapine for all indications, and we will maintain exclusive rights to manufacture and sell *Staccato* alprazolam and *Staccato* loxapine to Symphony Allegro or its sublicensee for those purposes. Pursuant to a warrant purchase agreement, we issued to Symphony Allegro Holdings, LLC a warrant with a five-year term to purchase 2,000,000 shares of our common stock at $9.91 per share, also paid a transaction structuring fee of $2.5 million, and reimbursed approximately $329,000 of Symphony Allegro transaction fees.

We have retained all other rights to our product candidates and the *Staccato* system. We are seeking a partner in the United States for our lead product candidate, AZ-004, and intend to retain co-promotion rights in the United States. We eventually plan to build a United States-based specialty sales force to commercialize our product candidates which are approved for marketing and which are intended for specialty pharmaceutical markets. We plan to enter into strategic partnerships with other companies to commercialize products that are intended for certain markets in the United States and for all of our product candidates in geographic territories outside the United States.

In March 2008, we obtained a committed equity line of credit under which we may sell, subject to certain limitations, up to $50 million of our registered common stock to Azimuth Opportunity, Ltd., or Azimuth, over a 24-month period. We are not obligated to utilize any of the $50 million equity line of credit. We will determine, at our sole discretion, the timing, the dollar amount and the price per share of each draw under this equity line of credit, subject to certain conditions. When and if we elect to use the equity line of credit, we will issue shares to Azimuth at a discount between 4.15% and 6.00% to the volume weighted average price of our common stock over a preceding period of trading days. Azimuth is not required to purchase any shares at a price below $5.00 per share. Any shares sold under this facility will be sold pursuant to a shelf registration statement declared effective by the Securities and Exchange Commission, or the SEC, on April 16, 2007. We have not sold any shares under this agreement as of December 31, 2008.

In March 2008, we sold 1,250,000 shares of our registered common stock to Biomedical Sciences Investment Fund Pte. Ltd, or Bio*One, at a price of $8.00 per share and issued a warrant to Bio*One to purchase up to $3 million of additional shares of our common stock at an exercise price of $8.00 per share. The agreement contained certain conditions, in which Bio*One was eligible to receive 135,041 additional shares of our registered common stock and an adjustment to the exercise price of the warrant, which would adjust the effective purchase price paid or payable by Bio*One to $7.22 per share. We did not meet these conditions, and in January 2009 we issued Bio*One 135,041 additional registered shares of our common stock and the warrant's exercise price was automatically adjusted to give Bio*One the right to purchase 415,522 shares at a $7.22 per share exercise price. In addition, we committed to initiate and maintain manufacturing operations in Singapore. The warrant became exercisable only if we terminated operations in Singapore or did not achieve certain performance milestones. In December 2008, we did not achieve a specified performance milestone, at which time the warrant became fully exercisable. All securities sold to Bio*One were sold pursuant to a shelf registration statement declared effective by the SEC on April 16, 2007.

We were incorporated December 19, 2000. We have funded our operations primarily through the sale of equity securities, capital lease and equipment financings and government grants. We have generated $7.4 million in revenues from inception through December 31, 2008, substantially all of which was earned through United States Small Business Innovation Research grants and the agreement with Endo. We had $486,000 of revenues in 2008 and no revenues in 2007. In the third quarter of 2008, we began to recognize revenues related to our Endo license agreement. In prior years we have recognized governmental grant revenue and drug compound feasibility revenue, however, we expect no grant revenue or drug compound feasibility screening revenue in 2009. In January 2009, we and Endo mutually terminated the license agreement, at which time we fully fulfilled our obligations under the agreement, and will recognize the remaining $9.5 million of deferred revenues into revenues in the first quarter of 2009. We do not expect any material product revenue until at least 2011.

We have incurred significant losses since our inception. As of December 31, 2008, our deficit accumulated during development stage was $222.6 million and total stockholders' equity was $33.7 million. We recognized net losses of $58.5 million, $45.1 million, and $41.8 million, in 2008, 2007 and 2006, respectively. We expect our net losses to continue, however, at a lower rate than 2008, as we continue our existing and planned preclinical studies and clinical trials, reduce our research and development efforts, continue our manufacturing development, and begin commercialization development. We expect that our general and administrative expenses in 2009 to slightly decrease from 2008 levels as we reduced our headcount in January 2009 and have otherwise sought to reduce expenses for items such as travel and outside consultancy.

The process of conducting preclinical studies and clinical trials necessary to obtain FDA approval is costly and time consuming. We consider the development of our product candidates to be crucial to our long term success. If we do not complete development of our product candidates and obtain regulatory approval to market one or more of these product candidates, we may be forced to cease operations. The probability of success for each product candidate may be impacted by numerous factors, including preclinical data, clinical data, competition, device development, manufacturing capability, regulatory approval and commercial viability. Our strategy is to focus our resources on AZ-004. We expect to file an NDA for this product candidate in the first quarter of 2010. We have announced that we are seeking partnerships to continue development of our other programs. If in the future we enter into additional partnerships, third parties could have control over preclinical development or clinical trials for some of our product candidates. Accordingly, the progress of such product candidate would not be under our control. We cannot forecast with any degree of certainty which of our product candidates, if any, will be subject to any future partnerships or how such arrangements would affect our development plans or capital requirements.

As a result of the uncertainties discussed above, the uncertainty associated with clinical trial enrollments, and the risks inherent in the development process, we are unable to determine the duration and completion costs of the current or future clinical stages of our product candidates or when, or to what extent, we will generate revenues from the commercialization and sale of any of our product candidates. Development timelines, probability of success and development costs vary widely. While we are currently focused on developing our product candidates, we anticipate that we and our partners, will make determinations as to which programs to pursue and how much funding to direct to each program on an ongoing basis in response to the scientific and clinical success of each product candidate, as well as an ongoing assessment as to the product candidate's commercial potential. We do not expect any of our current product candidates to be commercially available before 2011, if at all.

In January 2009, we consolidated our operations to primarily focus our efforts on the continued rapid development of AZ-004. As part of the reorganization, we reduced our total workforce by 33% and we mutually agreed with Endo to terminate our development agreement for our AZ-003 product. We anticipate that this consolidation will reduce 2009 operating expenses by $21.5 million from the 2008 operating expenses. We anticipate that with current cash, cash equivalents and marketable securities along with interest earned thereon, expected payments from Symphony Allegro, the proceeds from option exercises, and purchases of common stock pursuant to our Employee Stock Purchase Plan, we will be able to maintain our currently planned operations into the second quarter of 2010. Changing circumstances may cause us to consume capital significantly faster or slower than we currently anticipate.

Critical Accounting Estimates and Judgments

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as reported revenues and expenses during the reporting periods. On an ongoing basis, we evaluate our estimates and judgments related to development costs. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making assumptions about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in Note 2 of the notes to consolidated financial statements, we believe the following accounting policies are critical to the process of making significant estimates and judgments in preparation of our financial statements.

Preclinical Study and Clinical Trial Accruals

We estimate our preclinical study and clinical trial expenses based on our estimates of the services received pursuant to contracts with multiple research institutions and clinical research organizations that conduct and manage preclinical studies and clinical trials on our behalf. The financial terms of these agreements vary from contract to contract and may result in uneven payment flows. Preclinical study and clinical trial expenses include the following:

- fees paid to contract research organizations in connection with preclinical studies;
- fees paid to contract research organizations and other clinical sites in connection with clinical trials; and
- fees paid to contract manufacturers in connection with the production of components and drug materials for preclinical studies and clinical trials.

We record accruals for these preclinical study and clinical trial costs based upon the estimated amount of work completed. All such costs are charged to research and development expenses based on these estimates. Costs related to patient enrollment in clinical trials are accrued as patients are entered in the trial. We monitor patient enrollment levels and related activities to the extent possible through internal reviews, correspondence and discussions with research institutions and organizations. However, if we have incomplete or inaccurate information, we may underestimate or overestimate activity levels associated with various preclinical studies and clinical trials at a given point in time. In this event, we could record significant research and development expenses in future periods when the actual activity level becomes known. To date, we have not made any material adjustments to our estimates of preclinical study and clinical trial costs. We make good faith estimates which we believe to be accurate, but the actual costs and timing of clinical trials are highly uncertain, subject to risk and may change depending upon a number of factors, including our clinical development plan. With the our ongoing Phase 3 clinical trial and future Phase 3 clinical trials, the process of estimating clinical trial costs will become more difficult as the trials will involve larger numbers of patients and clinical sites.

Share-Based Compensation

On January 1, 2006, we adopted the fair value recognition provisions of Statement of Financial Accounting Standard No. 123R, *Share-Based Payment*, or SFAS 123R. As required, we adopted SFAS 123R using the prospective transition method. Under this transition method, beginning January 1, 2006, compensation cost recognized includes: (a) compensation cost for share-based payments granted prior to, but not yet vested as of December 31, 2005 related to (i) employees, based on the intrinsic value in accordance with the provisions of Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees*, or APB 25, and (ii) non-employees based on the options fair value in accordance with the provisions of SFAS 123, and (b) compensation cost for all share-based payments granted or modified subsequent to December 31, 2005, based on the grant-date fair value estimated in accordance with the provisions of SFAS 123R.

We currently use the Black-Scholes option pricing model to determine the fair value of stock options and purchase rights issued under the employee stock purchase plan. The determination of the fair value of share-based payment awards on the date of grant using an option-pricing model is affected by our stock price as well as assumptions regarding a number of complex and subjective variables. These variables include our expected stock price volatility over the term of the awards, actual and projected employee stock option exercise behaviors, risk-free interest rates and expected dividends.

The estimated fair value of restricted stock unit awards is calculated based on the market price of our common stock on the date of grant, reduced by the present value of dividends expected to be paid on our common stock prior to vesting of the restricted stock unit. Our current estimate assumes no dividends will be paid prior to the vesting of the restricted stock unit.

Through 2007, we estimated the expected term of options using the "simplified" method, as illustrated in SAB 107. Beginning in 2008, we estimated the expected term of options based on the historical term periods of options that have been granted but are no longer outstanding and the estimated terms of outstanding options.

As we had been operating as a public company for a period of time that was significantly shorter than our estimated expected option term, we were unable to use actual price volatility data. Therefore, we estimated the volatility of our common stock based on volatility of similar entities through 2007. In 2008 we estimated the volatility of our stock based on our actual historical volatility since our initial public offering.

We base the risk-free interest rate that we use in the option pricing model on U.S. Treasury zero-coupon issues with remaining terms similar to the expected term on the options. We do not anticipate paying any cash dividends in the foreseeable future and therefore use an expected dividend yield of zero in the option pricing model.

We are required to estimate forfeitures at the time of grant and revise those estimates in subsequent periods if actual forfeitures differ from those estimates. We use historical data to estimate pre-vesting option forfeitures and record share-based compensation expense only for those awards that are expected to vest. All share-based payment awards are amortized on a straight-line basis over the requisite service periods of the awards, which are generally the vesting periods.

If factors change and we employ different assumptions for estimating share-based compensation expense in future periods or if we decide to use a different valuation model, the expenses in future periods may differ significantly from what we have recorded in the current period and could materially affect our operating loss, net loss and net loss per share.

See Note 2 to the consolidated financial statements in this Annual Report on Form 10-K for further information regarding the SFAS 123R disclosures.

Symphony Allegro, Inc.

On December 1, 2006 we entered into a transaction involving a series of related agreements with Symphony Capital LLC, or Symphony Capital, Symphony Allegro Holdings LLC, or Holdings, and Holdings' wholly owned subsidiary Symphony Allegro, Inc., or Allegro, to fund the clinical development of AZ-002, *Staccato* alprazolam, and AZ-004/104, *Staccato* loxapine, or the programs. Symphony Capital and other investors, together referred to as Symphony, invested $50 million in Holdings, which then invested the $50 million in Allegro. Pursuant to the agreements, Allegro agreed to invest up to the full $50 million to fund the clinical development of the programs, and we licensed to Allegro certain intellectual property rights related to these programs. We have retained manufacturing rights to these product candidates. Pursuant to the agreements, we continue to be primarily responsible for all preclinical, clinical and device development efforts as well as maintenance of the intellectual property portfolio for the programs. We and Allegro have established a development committee to oversee the programs. We participate in the development committee and have the right to appoint one of the five board of director seats of Allegro. We have incurred and may continue to incur expenses related to the programs that are not funded by Allegro. Pursuant to the agreements, we have received an exclusive purchase option, or the purchase option, that gives us the right, but not the obligation, to acquire all, but not less than all, of the equity of Allegro, and reacquire the intellectual property rights that we licensed to Allegro. The purchase option is exercisable at predetermined prices that increase over time and range from $67.5 million starting December 31, 2007 to $122.5 million through December 1, 2010. As of March 1, 2009 the purchase option is $92.5 million. The purchase option exercise price may be paid for in cash or in a combination of cash and our common stock, in our sole discretion, provided that the common stock portion may not exceed 40% of the purchase option exercise price or 10% of our common stock issued and outstanding as of the purchase option closing date. If we pay a portion of the purchase option exercise price in shares of our common stock, then we will be required to register such shares for resale under a resale registration statement pursuant to the terms of a registration rights agreement. If we do not exercise the purchase option by December 1, 2010, then Allegro will retain its exclusive license to develop and commercialize *Staccato* alprazolam and *Staccato* loxapine for all indications, and, if they are ultimately commercialized, we will maintain exclusive rights to manufacture and sell *Staccato* alprazolam and *Staccato* loxapine to Allegro or its sublicensee for those purposes. In consideration for the purchase option, we issued to Holdings a five-year warrant to purchase 2,000,000 shares of our common stock at $9.91 per share and paid $2.85 million for structuring fees and related expenses to Symphony Capital.

Under FASB Interpretation No. 46, *Consolidation of Variable Interest Entities*, or FIN 46R, a variable interest entity, or VIE, is (1) an entity that has equity that is insufficient to permit the entity to finance its activities without additional subordinated financial support, or (2) an entity that has equity investors that cannot make significant decisions about the entity's operations or that do not absorb their proportionate share of the expected losses or do not receive the expected residual returns of the entity. FIN 46R requires a VIE to be consolidated by the party that is deemed to be the primary beneficiary, which is the party that has exposure to a majority of the potential variability in the VIE's outcomes. The application of FIN 46R to a given arrangement requires significant management judgment.

We have consolidated the financial position and results of operations of Allegro in accordance with FIN 46R. We believe Allegro is by design a VIE because we have a purchase option to acquire its outstanding voting stock at prices that are fixed based upon the date the option is exercised. The fixed nature of the purchase option price limits Symphony's returns, as the investor in Allegro.

FIN 46R deems parties to be de facto agents if they cannot sell, transfer, or encumber their interests without the prior approval of an enterprise. Symphony Capital is considered to be a de facto agent of ours pursuant to this provision, and because we and Symphony, as a related party group, absorb a majority of Allegro's variability, we evaluated whether, pursuant to FIN 46R's requirements, we are most closely associated with Allegro. We concluded that we are most closely associated with Allegro and should consolidate Allegro because (1) we originally developed the technology that was assigned to Allegro, (2) we will continue to oversee and monitor the development program, (3) our employees will continue to perform substantially all of the development work, (4) we significantly influenced the design of the responsibilities and corporate structure of Allegro, (5) Allegro's operations are substantially similar to our activities, and (6) through the purchase option, we have the ability to meaningfully participate in the benefits of a successful development effort.

Symphony Capital will be required to absorb the development risk for its equity investment in Allegro. Pursuant to FIN 46R's requirements, Symphony Capital's equity investment in Allegro is classified as non-controlling interest in our consolidated balance sheets. The noncontrolling interest held by Symphony Capital has been reduced by the $10.7 million fair value of the warrant it received in consideration for the purchase option and $2.85 million of fees we immediately paid to Symphony Capital upon the transaction's closing because the total consideration provided by us to Symphony Capital effectively reduces Symphony Capital's at-risk equity investment in Allegro. While we perform the research and development on behalf of Allegro, our development risk is limited to the consideration we provided to Symphony Capital (the warrant and fees).

Losses incurred by Allegro are charged to the noncontrolling interest until that balance has been reduced to zero, at which point our net loss will be increased for the research and development expenses incurred subsequent to that date. Net losses incurred by Allegro and charged to the noncontrolling interest were $18.6 million and $10.8 million for the years ended December 31, 2008 and 2007, respectively. At December 31, 2008, the noncontrolling interest balance was $5.4 million. As of December 31, 2008, the investments held by Allegro were $21.3 million, which we expect to spend during the period ending March 31, 2010.

In December 2007, the FASB issued SFAS No. 160, *Noncontrolling Interests in Consolidated Financial Statements — An Amendment of ARB No. 5*, or SFAS 160. SFAS 160 will require that noncontrolling interests in subsidiaries be reported as a component of stockholders' equity in the consolidated balance sheet. SFAS 160 also requires that earnings or losses attributed to the noncontrolling interests be reported as part of consolidated earnings and not as a separate component of income or expense, as well as requires disclosure of the attribution of consolidated earnings to the controlling and noncontrolling interests on the face of the consolidated statement of operations. SFAS 160 is effective for fiscal years beginning after December 15, 2008.

If the purchase option expires unexercised, we would then be required to deconsolidate Allegro. That potential deconsolidation would not be expected to impact our earnings because the carrying value of the net assets of Allegro would be expected to be zero. In contrast, if we exercise the purchase option, we will retain control of Allegro. As such, we would expect to record the exercise of the purchase option as a return to the noncontrolling interest. We do not expect to recognize an asset for the purchase option payment to be made to Symphony. Instead, the payment is expected to be accounted for as a capital transaction (that is, a return to the noncontrolling interest) that would not affect our net income or loss. However, because the exercise of the purchase option will be accounted for as a capital transaction, it will be treated as a deemed dividend for purposes of reporting earnings per share, increasing loss per

share or decreasing income per share, as the case may be, in the period we exercise the purchase option. If the programs are successful and the resources are available, we expect to exercise the purchase option.

Revenue Recognition

We recognize revenue in accordance with the SEC Staff Accounting Bulletin (SAB) No. 101, *Revenue Recognition in Financial* Statements, or SAB 101, as amended by Staff Accounting Bulletin No. 104, *Revision of Topic 13.* or SAB 104.

In determining the accounting for collaboration agreements, we follow the provisions of Emerging Issues Task Force (EITF) Issue 00-21, *Revenue Arrangements with Multiple Deliverables*, or EITF 00-21. EITF 00-21 provides guidance on whether an arrangement involves multiple revenue-generating deliverables that should be accounted for as a single unit of accounting or divided into separate units of accounting for revenue recognition purposes and, if this division is required, how the arrangement consideration should be allocated among the separate units of accounting. If the arrangement represents a single unit of accounting, the revenue recognition policy and the performance obligation period must be determined (if not already contractually defined) for the entire arrangement. If the arrangement represents separate units of accounting according to the EITF's separation criteria, a revenue recognition policy must be determined for each unit.

Revenues for non-refundable upfront license fee payments, where we continue to have obligations, will be recognized as performance occurs and obligations are completed. We recorded the $10 million upfront fee paid by Endo as deferred revenue and began to recognize this revenue in the third quarter of 2008. Through December 31, 2008, we have recognized $486,000 in revenue in connection with the Endo upfront fee. In January 2009, we mutually agreed with Endo to terminate the agreement. Upon the termination of the agreement all of the rights to AZ-003 reverted to us. We will recognize the remaining $9.5 million payment as revenue in the first quarter of 2009.

Results of Operations

Comparison of Years Ended December 31, 2008 and 2007

Revenue. We had $486,000 of revenues in 2008 and no revenues in 2007. In the third quarter of 2008, we began to recognize revenues related to our Endo license agreement. In prior years we have recognized governmental grant revenue and drug compound feasibility revenue, however, we expect no grant revenue or drug compound feasibility screening revenue in 2009. In January 2009, we mutually agreed with Endo to terminate the license agreement, at which time we fulfilled our obligations under the license agreement, and will recognize the remaining $9.5 million of deferred revenues into revenues in the first quarter of 2009.

Operating Expenses

Our operating expenses were affected by our prospective method of adoption of SFAS 123R. As a result, we believe reviewing our operating expenses both inclusive and exclusive of share-based compensation provides a better understanding of the growth of our operations. The impact of share-based compensation on operating expenses is outlined as follows (in thousands):

	Year Ended December 31,		
	2008	2007	2006
Non share-based compensation expenses:			
Research and development	$58,639	$43,760	$34,724
General and administrative	15,121	13,357	9,522
Total non share-based compensation expenses	73,760	57,117	44,246
Share-based compensation expenses:			
Research and development	2,926	1,885	1,770
General and administrative	2,520	1,531	447
Total share-based compensation expenses	5,446	3,416	2,217
Total operating expenses	$79,206	$60,533	$46,463

Research and Development Expenses. Research and development expenses consist of costs associated with research activities, as well as costs associated with our product development efforts, conducting preclinical studies and clinical trials and manufacturing development efforts. All research and development costs, including those funded by third parties, are expensed as incurred. Research and development expenses include:

- external research and development expenses incurred under agreements with third party contract research organizations and investigational sites where a substantial portion of our preclinical studies and all of our clinical trials are conducted;
- third party supplier, consultant and employee related expenses, which include salary and benefits;
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, depreciation of leasehold improvements and equipment and laboratory and other supplies; and
- in 2006, certain incremental charges related to officer loan extinguishments and non-cash stock-based compensation expense.

The table below sets forth our research and development expenses since January 1, 2003 and cumulative expenses for each of our lead product candidates based on our internal records and estimated allocations of employee time and related expenses:

	Year Ended December 31,					
Preclinical and Clinical Development:	**2008**	**2007**	**2006**	**2005**	**2004**	**From December 19, 2000 (Inception) Through December 31, 2008.**
			(In thousands)			
AZ-004/104	$26,789	$15,524	$ 6,073	$ 3,187	$ 119	$ 51,692
AZ-003	17,070	1,474	3,687	5,021	1,706	29,894
AZ-001	1,151	8,163	9,535	6,369	8,640	39,372
AZ-002	1,898	3,795	3,094	3,803	1,930	15,010
AZ-007	1,773	8,214	2,384	—	—	12,371
Other preclinical programs	—	—	3,243	—	—	3,243
Total preclinical and clinical development	48,681	37,170	28,016	18,380	12,395	151,582
Research	12,884	8,475	8,478	7,855	2,752	53,101
Total research and development	$61,565	$45,645	$36,494	$26,235	$15,147	$204,683

Research and development expenses increased 35% to $61.6 million in 2008 from $45.6 million in 2007. The increases were due primarily to:

- increased spending on our AZ-004/104 product candidates as we continued development of these product candidates under the Symphony Allegro agreement, including our first Phase 3 clinical trial of AZ-004 which began enrollment in February 2008 and completed enrollment in June 2008 and our second Phase 3 clinical trial of AZ-004 which began enrollment in July 2008 and completed enrollment in October 2008,
- increased spending on our AZ-003 product candidate as we continued development of this product candidate under the Endo agreement, and
- increased research expenses as we increased our device development and manufacturing process scale-up efforts.

These increases were partially offset by decreased spending on:

- our AZ-001 product candidate due to Phase 2b clinical trial efforts and ongoing non clinical efforts occurring in 2007,
- our AZ-002 product candidate due to higher development and manufacturing efforts to modify the AZ-002 device and manufacture clinical trial materials for the Phase 2a trial in 2007, and
- our AZ-007 product candidate due to the preclinical and regulatory efforts in 2007 to support and prepare the IND filing that occurred in the fourth quarter of 2007.

We expect that research and development expenses will decrease in 2009 as we expect lower clinical trial expenses for AZ-004/AZ-104, a result of our completing two Phase 3 trials for AZ-004 in 2008. We also expect lower employee related costs in 2009, a result of our headcount reduction in the first quarter of 2009. We do not expect to expend any substantial amounts on AZ-003 in 2009. We also expect our expenses for AZ-001, AZ-002, and AZ-007 to be lower in 2009 as we do not intend to continue development of these programs unless we can partner the programs.

General and Administrative Expenses. General and administrative expenses consist principally of salaries and related costs for personnel in executive, finance, accounting, business development, legal and human resources functions. Other general and administrative expenses include facility and information technology costs not otherwise included in research and development expenses, patent related costs and professional fees for legal, consulting and accounting services.

General and administrative expenses increased 18% to $17.6 million in 2008 from $14.9 million in 2007. The increases were primarily due to increased staffing to manage and support our growth resulting in increased payroll and related expenses, increased third party intellectual property expenses as we continued to increase and maintain our intellectual property portfolio, and higher facilities expenses to support our growth.

We expect that our general and administrative expenses in 2009 to slightly decrease from 2008 levels due to a headcount reduction in January 2009 and our efforts to reduce expenses for items such as travel and outside consultancy.

Interest and Other Income, Net. Interest and other income, net, primarily represents income earned on our cash, cash equivalents, marketable securities balances, and marketable securities held by Symphony Allegro. Interest and other income, net was $2.6 million for 2008 and $5.6 million for 2007. The decrease was primarily due to lower average cash, cash equivalent and marketable securities balances and lower interest rates earned on such balances. We expect interest income to continue to decrease in future periods as we expect our cash, cash equivalent and marketable securities balances to decrease as we continue to incur net losses.

Interest Expense. Interest expense represents interest on our equipment loans and was $0.9 million in 2008 and $1.0 million in 2007. The decrease was primarily due to decreases in our equipment loan borrowings as we made no additional borrowing under our equipment financing agreements in 2008.

Loss Attributed to Noncontrolling Interest in Symphony Allegro. Pursuant to the agreements that we entered into with Symphony Allegro, Inc. in December 2006, we consolidate Symphony Allegro's financial condition and results of operations in accordance with FASB Interpretation No. 46R, *Consolidation of Variable Interest Entities an Interpretation of Accounting Research Bulletin No. 51,* or FIN 46R. Accordingly, we have deducted the losses attributable to the noncontrolling interest from our net loss in the consolidated statement of operations, and we have also reduced the noncontrolling interest holders' ownership interest in Symphony Allegro, Inc. in the consolidated balance sheet by the loss attributed to the noncontrolling interests in Symphony Allegro, Inc. The losses attributed to the noncontrolling interest holders was $18.6 million in 2008 and $10.8 million in 2007. The increase was primarily due to increased spending on AZ-004, primarily the result of the two Phase 3 clinical trials in 2008.

Comparison of Years Ended December 31, 2007 and 2006

Revenue. We had no revenues in 2007 and had $1.0 million of revenues in 2006. In 2006, we recognized approximately $1.0 million of government grant revenue and $30,000 of revenue from drug compound feasibility screening.

Operating Expenses

Research and Development Expenses. Research and development expenses increased 25% to $45.6 million in 2007 from $36.5 million in 2006. The increases were due primarily to:

- increased spending on our AZ-004/104 and AZ-002 product candidates as we continued development of these product candidates under the Symphony Allegro agreement, including the launch of a Phase 2a clinical trial of AZ-104 at the end of the second quarter of 2007, and
- the increased spending on our AZ-007 product candidate.

These increased efforts were partially offset by decreased spending on:

- our AZ-001 product candidate due to the completion of the Phase 2b clinical trial in the first quarter of 2007,
- our AZ-003 product candidate, as we significantly reduced development on this program until we obtained a developmental partner, and
- our other preclinical development as we focused our efforts on our AZ-007 product candidate.

General and Administrative Expenses. General and administrative expenses consist principally of salaries and related costs for personnel in executive, finance, accounting, business development, legal and human resources functions. Other general and administrative expenses include facility and information technology costs not otherwise included in research and development expenses, patent related costs and professional fees for legal, consulting and accounting services.

General and administrative expenses increased 49% to $14.9 million in 2007 from $10.0 million in 2006. The increase was primarily due to expanding legal and accounting staff, adding infrastructure and incurring additional costs related to operating as a public company, investor relations programs, increased director fees, increased professional fees and non-cash stock-based compensation expense.

Interest and Other Income, Net. Interest and other income, net, primarily represents income earned on our cash, cash equivalents, marketable securities balances, and marketable securities held by Symphony Allegro. Interest and other income, net was $5.6 million for 2007 and $2.7 million for 2006. The increase was primarily due to higher average cash, cash equivalent and marketable securities balances due to our public stock offering in May 2007, and the addition of investments held by Symphony Allegro, Inc in December 2006.

Interest Expense. Interest expense represents interest on our equipment loans and was $1.0 million in 2007 and $0.8 million in 2006. The increase was primarily due to increases in our equipment loan borrowings.

Loss Attributed to Noncontrolling Interest in Symphony Allegro. The losses attributed to the noncontrolling interest holders was $10.8 million in 2007 and $1.7 million in 2006. The increase was primarily due to a full year of Symphony Allegro losses in 2007 compared to one month of losses in 2006 and the timing of expenses incurred on the AZ-004 and AZ-104 clinical trials.

Liquidity and Capital Resources

Since inception, we have financed our operations primarily through private placements and public offerings of equity securities, receiving aggregate net proceeds from such sales totaling $120.7 million, revenues primarily from government grants and totaling $7.4 million, payments from Symphony Allegro and an upfront fee from Endo in the amount of $10 million. We have received additional funding from equipment financing obligations, interest earned on investments, as described below, and funds received upon exercises of stock options and exercises of purchase rights under our Employee Stock Purchase Plan. As of December 31, 2008, we had $37.6 million in cash, cash equivalents and marketable securities and $21.3 million of marketable securities held by Symphony Allegro. The

marketable securities held by Symphony Allegro are used to fund the development of AZ-002, AZ-004 and AZ-104 and are not available for general corporate expenses. Our cash and marketable security balances are held in a variety of interest bearing instruments, including obligations of United States government agencies, high credit rating corporate borrowers and money market accounts. Investments held by Symphony Allegro consist of investments in a money market fund that invests primarily in domestic commercial paper, securities issued or guaranteed by the U.S. government or its agencies, U.S. and Yankee bank obligations and fully collateralized repurchase agreements. Cash in excess of immediate requirements is invested with regard to liquidity and capital preservation.

Net cash used in operating activities was $55.1 million, $35.8 million, and $33.3 million in 2008, 2007 and 2006, respectively. The net cash used in each of these periods primarily reflects net loss for these periods, offset in part by depreciation, non-cash stock-based compensation, loss attributed to noncontrolling interests, and non-cash changes in operating assets and liabilities. In 2008, the large decrease in other receivables was due to the collection of a receivable of $10.0 million from Endo in January 2008 related to the license agreement signed in December 2007 and a $2.1 million receivable related to the reimbursement of leasehold improvements from the landlord of our Mountain View facility in May 2008. In 2007, the large increase in other receivables was affected by the above mentioned receivable from Endo and the receivable relating to tenant improvements, which were outstanding in 2007 and collected in 2008. In 2007, the increase in other liabilities is primarily due to $10.0 million of deferred revenues related to the Endo license agreement, and $14.3 million of leasehold improvement reimbursements from the Mountain View landlord recorded as deferred rent in 2007.

Net cash provided by (used in) investing activities was $42.8 million, $(20.0) million, and $(61.4) million in 2008, 2007 and 2006, respectively. Investing activities consist primarily of purchases and maturities of marketable securities and capital purchases. During 2008 we had maturities, net of purchases, of marketable securities of $27.2 million. During 2007 and 2006 we purchased $11.4 million and $2.9 million of marketable securities, net of maturities, respectively. In 2006, we also had net purchases of $50.0 million of investments by Symphony Allegro. Purchases of property and equipment were $2.7 million, $19.1 million, and 8.1 million, in 2008, 2007 and 2006, respectively, of which $16.5 million of property and equipment purchases in 2007 related to the build out of our leased facility in Mountain View, California.

Net cash provided by financing activities was $6.9 million, $70.1 million, and $94.9 million in 2008, 2007 and 2006, respectively. Financing activities consist primarily of proceeds from the sale of our common stock, issuance of a noncontrolling interest, and equipment financing arrangements. In 2008, 2007 and 2006, we received net proceeds from the issuance of common stock of $11.2 million, $67.8 million and $46.0 million, respectively. In 2006, we received net proceeds of $47.2 from purchase of noncontrolling interests by preferred shareholders in Symphony Allegro, net of fees. In 2008, payments on equipment financing arrangements were $4.2 million. Proceeds from equipment financing arrangements, net of payments, were $2.3 million and $1.8 million during 2007 and 2006, respectively. There were no borrowings under any equipment financing arrangements in 2008.

We believe that with current cash, cash equivalents and marketable securities along with interest earned thereon, the expected payments from Symphony Allegro, the proceeds from option exercises, and purchases of common stock pursuant to our Employee Stock Purchase Plan, we will be able to maintain our currently planned operations into the second quarter of 2010. Changing circumstances may cause us to consume capital significantly faster or slower than we currently anticipate. We have based these estimates on assumptions that may prove to be wrong, and we could utilize our available financial resources sooner than we currently expect. The key assumptions underlying these estimates include:

- expenditures related to continued preclinical and clinical development of our lead product candidates during this period within budgeted levels;
- the timing and amount of payments from Symphony Allegro;
- no unexpected costs related to the development of our manufacturing capability; and
- no growth in the number of our employees during this period.

Our forecast of the period of time that our financial resources will be adequate to support operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number

of factors, including the factors discussed in "Risk Factors." In light of the numerous risks and uncertainties associated with the development and commercialization of our product candidates and the extent to which we enter into strategic partnerships with third parties to participate in their development and commercialization, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated clinical trials. Our future funding requirements will depend on many factors, including:

- the scope, rate of progress, results and costs of our preclinical studies, clinical trials and other research and development activities;
- the terms and timing of any distribution, strategic partnerships or licensing agreements that we may establish;
- the terms and timing of any repurchase of rights from Symphony Allegro, which ranges from $92.5 million at March 31, 2009 to $122.5 million through December 1, 2010;
- our ability to draw on our equity line of credit with Azimuth;
- the cost, timing and outcomes of regulatory approvals;
- the number and characteristics of product candidates that we pursue;
- the cost and timing of establishing manufacturing, marketing and sales capabilities;
- the cost of establishing clinical and commercial supplies of our product candidates;
- the cost of preparing, filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights; and
- the extent to which we acquire or invest in businesses, products or technologies, although we currently have no commitments or agreements relating to any of these types of transactions.

In March 2008, we obtained a committed equity line of credit under which we may sell, subject to certain limitations, up to $50 million of our registered common stock to Azimuth Opportunity, Ltd., or Azimuth, over a 24-month period. We are not obligated to utilize any of the $50 million equity line of credit. We will determine, at our sole discretion, the timing, the dollar amount and the price per share of each draw under this equity line of credit, subject to certain conditions. When and if we elect to use the equity line of credit, we will issue shares to Azimuth at a discount between 4.15% and 6.00% to the volume weighted average price of our common stock over a preceding period of trading days. Azimuth is not required to purchase any shares at a price below $5.00 per share. At February 27, 2009, our stock price was $1.60.

We will need to raise additional funds to support our operations, and such funding may not be available to us on acceptable terms, or at all. If we are unable to raise additional funds when needed, we may not be able to continue development of our product candidates or we could be required to delay, scale back or eliminate some or all of our development programs and other operations. We may seek to raise additional funds through public or private financing, strategic partnerships or other arrangements. Any additional equity financing may be dilutive to stockholders and debt financing, if available, may involve restrictive covenants. If we raise funds through collaborative or licensing arrangements, we may be required to relinquish, on terms that are not favorable to us, rights to some of our technologies or product candidates that we would otherwise seek to develop or commercialize ourselves. Our failure to raise capital when needed may harm our business, financial condition, results of operations, and prospects.

Contractual Obligations

We lease two buildings with an aggregate of 106,894 square feet of manufacturing, office and laboratory facilities in Mountain View, California, which we began to occupy in the fourth quarter of 2007. We currently occupy 87,560 square feet of these facilities and sublease the remaining 19,334 square feet. The lease for both facilities expires on March 31, 2018, and we have two options to extend the lease for five years each. Our sublease agreement expires on April 30, 2009.

We have financed a portion of our equipment purchases through various equipment financing agreements. Under the agreements, equipment advances are to be repaid in 36 to 48 monthly installments of principal and interest. The interest rate, which is fixed for each draw, is based on the U.S. Treasuries of comparable maturities and ranges from 9.2% to 10.6%. The equipment purchased under the equipment financing agreement is pledged as security.

Our future contractual payments, net of sublease income, including interest at December 31, 2008 are as follows (in thousands):

	Payments Due by Period				
Contractual Obligations	Total	Less Than 1 Year	1-3 Years	3-5 Years	Thereafter
			(In thousands)		
Equipment financing obligations	$ 7,264	$4,595	$ 2,669	$ —	$ —
Operating lease obligations	45,686	4,558	10,154	10,182	20,792
Total	$52,950	$9,153	$12,823	$10,182	$20,792

On November 2, 2007, we entered into a manufacturing and supply agreement, or the supply agreement, with Autoliv ASP, Inc, or Autoliv, relating to the commercial supply of chemical heat packages that can be incorporated into our *Staccato* device. Autoliv had developed these chemical heat packages for us pursuant to a development agreement between Autoliv and us executed in October 2005. Under the terms of the supply agreement, Autoliv will develop a manufacturing line capable of producing 10 million chemical heat packages a year. We will pay Autoliv $12 million upon the earlier of December 31, 2011 or 60 days after the approval by the Food and Drug Administration of a new drug application filed by us. If the agreement is terminated by either party, we will be required to reimburse Autoliv up to $12 million for certain expenses related to the equipment and tooling used in the production and testing of the chemical heat packages. Upon payment by us, Autoliv will be required to transfer possession and ownership of such equipment and tooling to us. Each quarter, with assistance from Autoliv, we estimate the amount of work performed on the development of the manufacturing line and recognize a portion of the total payment related to the manufacturing line as a capital asset and a corresponding non-current liability. As of December 31, 2008, we recorded a fixed asset and a non-current liability of $600,000 related to our commitment to Autoliv for the development of the manufacturing line. Autoliv has also agreed to manufacture, assemble and test the chemical heat packages solely for us in conformance with our specifications. We will pay Autoliv a specified purchase price, which varies based on annual quantities ordered by us, per chemical heat package delivered. The initial term of the supply agreement expires on December 31, 2012 and may be extended by written mutual consent.

Recently Adopted Accounting Pronouncements

Statement of Financial Accounting Standard No. 157 and Staff Position 157-2

Effective January 1, 2008, we adopted Statement of Financial Accounting Standard No. 157, *Fair Value Measurements,* or SFAS 157. SFAS 157 defines fair value, establishes a framework for measuring fair value in accordance with generally accepted accounting principles, and enhances disclosures about fair value measurements. We apply the provisions of SFAS 157 prospectively. Fair value is defined under SFAS 157 as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value under SFAS 157 must maximize the use of observable inputs and minimize the use of unobservable inputs. The standard describes a fair value hierarchy based on three levels of inputs, of which the first two are considered observable and the last unobservable, that may be used to measure fair value which are the following:

- *Level 1* — Quoted prices in active markets for identical assets or liabilities.
- *Level 2* — Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

- *Level 3* — Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

In February 2008, the FASB issued FASB Staff Position 157-2 *Partial Deferral of the Effective Date of Statement 157*, or FSP 157-2. FSP 157-2 delays the effective date of SFAS 157 for nonfinancial assets and nonfinancial liabilities, except for items that are recognized or disclosed at fair value in the financial statements on a recurring basis (at least annually) to fiscal years beginning after November 15, 2008.

In accordance with FSP 157-2, we deferred the adoption of FAS 157 for one year for nonfinancial assets and nonfinancial liabilities that are recognized or disclosed at fair value in the financial statements on a nonrecurring basis. The adoption of SFAS 157 for financial assets and financial liabilities, effective January 1, 2008, did not have a material effect on our consolidated financial position, operating results or cash flows. See Note 3 to the Consolidated Financial Statements.

Emerging Issues Task Force Issue No. 07-3

Effective January 1, 2008, we adopted the Emerging Issues Task Force, or EITF, Issue No. 07-3, or EITF 07-3, *Accounting for Nonrefundable Advance Payments for Goods or Services to Be Used in Future Research and Development Activities.* The scope of EITF 07-3 is limited to nonrefundable advance payments for goods and services to be used or rendered in future research and development activities pursuant to an executory contractual arrangement. This issue provides that nonrefundable advance payments for goods or services that will be used or rendered for future research and development activities should be deferred and capitalized. We adopted the provisions of EITF 07-3 prospectively for new contracts entered into on or after January 1, 2008. The adoption of the provisions of EITF 07-3 on January 1, 2008 did not have a material impact on our financial position, results of operations or cash flows.

Recently Issued Accounting Pronouncements

Statement of Financial Accounting Standard No. 141(R)

In December 2007, the FASB issued SFAS No. 141 (revised 2007), *Business Combinations*, or SFAS 141(R). This standard establishes principles and requirements for how an acquirer in a business combination recognizes and measures the identifiable assets acquired, the liabilities assumed and any noncontrolling interest in the acquiree in its financial statements. SFAS 141(R) also establishes principles and requirements for how an acquirer recognizes and measures the goodwill acquired in a business combination and it establishes disclosure requirements to facilitate an evaluation of the nature and financial effects of a business combination. SFAS 141(R) is effective for business combinations which occur during the first annual reporting period beginning on or after December 15, 2008. We expect the effect of adoption of this standard will be limited to any acquisitions made by us which close subsequent to December 31, 2008.

Statement of Financial Accounting Standard No. 160

In December 2007, the FASB issued SFAS No. 160, *Noncontrolling Interests in Consolidated Financial Statements — An Amendment of ARB No. 51*, or SFAS 160. SFAS 160 will require that noncontrolling interests in subsidiaries be reported as a component of stockholders' equity in the consolidated balance sheet. SFAS 160 also requires that earnings or losses attributed to the noncontrolling interests be reported as part of consolidated earnings and not as a separate component of income or expense, as well as requires disclosure of the attribution of consolidated earnings to the controlling and noncontrolling interests on the face of the consolidated statement of operations. SFAS 160 is effective for fiscal years beginning after December 15, 2008. Beginning with our first quarter of 2009, we will adopt these report requirements.

Off-Balance Sheet Arrangements

None.

Item 7A. ***Quantitative and Qualitative Disclosures About Market Risk***

Our exposure to market risk is confined to our cash, cash equivalents, which have maturities of less than three months, and marketable securities. The primary objective of our investment activities is to preserve our capital to fund operations. We also seek to maximize income from our investments without assuming significant risk. To achieve our objectives, we maintain a portfolio of cash equivalents and marketable securities in a variety of securities of high credit quality. As of December 31, 2008, we had cash, cash equivalents and marketable securities of $37.6 million and investments held by Symphony Allegro of $21.3 million. The securities in our investment portfolio are not leveraged, are classified as available for sale and are, due to their very short-term nature, subject to minimal interest rate risk. We currently do not hedge interest rate exposure. Because of the short-term maturities of our investments, we do not believe that an increase in market rates would have a material negative impact on the realized value of our investment portfolio. We actively monitor changes in interest rates. We perform quarterly reviews of our investment portfolio and believe we have minimal exposure related to mortgage and other asset backed securities and no exposure to auction rate securities.

Item 8. ***Financial Statements and Supplementary Data***

ALEXZA PHARMACEUTICALS, INC.

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders
Alexza Pharmaceuticals, Inc.

We have audited the accompanying consolidated balance sheets of Alexza Pharmaceuticals, Inc. (a development stage company) (the "Company") as of December 31, 2008 and 2007, and the related consolidated statements of operations, convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2008 and for the period from December 19, 2000 (inception) to December 31, 2008. These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Alexza Pharmaceuticals, Inc. (a development stage company) at December 31, 2008 and 2007, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2008 and for the period from December 19, 2000 (inception) to December 31, 2008, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Alexza Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2008, based on criteria established in Internal Control — Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 9, 2009 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Palo Alto, California
March 9, 2009

ALEXZA PHARMACEUTICALS, INC
(a development stage company)

CONSOLIDATED BALANCE SHEETS

	December 31, 2008	December 31, 2007
	(In thousands, except share and per share amounts)	
ASSETS		
Current assets:		
Cash and cash equivalents	$ 26,036	$ 31,337
Marketable securities	11,520	38,054
Investments held by Symphony Allegro, Inc.	21,318	39,449
Other receivables	—	12,055
Prepaid expenses and other current assets	1,130	1,377
Total current assets	60,004	122,272
Property and equipment, net	24,152	26,156
Restricted cash	400	604
Other assets	79	93
Total assets	$ 84,635	$ 149,125
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 4,928	$ 5,206
Accrued clinical trial liabilities	1,294	1,301
Other accrued liabilities	5,205	5,087
Deferred revenues	1,667	—
Current portion of equipment financing obligations	4,139	4,586
Total current liabilities	17,233	16,180
Deferred rent	17,386	16,685
Deferred revenue	7,847	10,000
Noncurrent portion of equipment financing obligations	2,515	6,317
Other noncurrent liabilities	600	—
Commitments (See Note 7)		
Non controlling interest in Symphony Allegro, Inc.	5,361	23,952
Stockholders' equity:		
Preferred stock, $0.0001 par value, 5,000,000 shares authorized at December 31, 2008 and 2007; no shares issued and outstanding at December 31, 2008 or 2007	—	—
Common stock, $0.0001 par value; 100,000,000 shares authorized at December 31, 2008 and 2007; 32,820,874 and 31,137,857 shares issued and outstanding at December 31, 2008 and 2007, respectively	3	3
Additional paid-in capital	256,426	240,681
Deferred stock compensation	(219)	(739)
Other comprehensive income	28	141
Deficit accumulated during development stage	(222,545)	(164,095)
Total stockholders' equity	33,693	75,991
Total liabilities and stockholders' equity	$ 84,635	$ 149,125

See accompanying notes.

ALEXZA PHARMACEUTICALS, INC.
(a development stage company)

CONSOLIDATED STATEMENTS OF OPERATIONS

	Year Ended December 31,			Period from December 19, 2000 (Inception) to December 31, 2008
	2008	2007	2006	
	(In thousands, except per share amounts)			
Revenue	$ 486	$ —	$ 1,028	$ 7,431
Operating expenses:				
Research and development	61,565	45,645	36,494	204,683
General and administrative	17,641	14,888	9,969	62,704
Acquired in-process research and development	—	—	—	3,916
Total operating expenses	79,206	60,533	46,463	271,303
Loss from operations	(78,720)	(60,533)	(45,435)	(263,872)
Interest and other income, net	2,614	5,626	2,687	13,806
Interest expense	(935)	(1,003)	(778)	(3,581)
Loss before non controlling interest in Symphony Allegro, Inc.	(77,041)	(55,910)	(43,526)	(253,647)
Loss attributed to non controlling interest in Symphony Allegro, Inc.	18,591	10,791	1,720	31,102
Net loss	$(58,450)	$(45,119)	$(41,806)	$(222,545)
Basic and diluted net loss per common share	$ (1.81)	$ (1.58)	$ (2.13)	
Shares used to compute basic and diluted net loss per common share	32,297	28,605	19,584	

See accompanying notes.

ALEXZA PHARMACEUTICALS, INC.
(a development stage company)

CONSOLIDATED STATEMENT OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)

	Convertible Preferred Stock		Preferred Stock		Common Stock		Additional Paid-In Capital	Stockholder Note Receivable	Deferred Stock Compensation	Other Comprehensive (Loss) Income	Deficit Accumulated During the Development Stage	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount						
	(In thousands, except share and per share amounts)											
Issuance of common stock to founders at $0.22 per share in December 2000 in exchange for technology and cash of $8	—	$ —	—	$—	454,536	$—	$ 100	$—	$—	$—	$ —	$ 100
Issuance of Series A preferred stock for cash at $0.40 per share in July 2001, net of issuance costs of $9	2,500,000	991	—	—	—	—	—	—	—	—	—	—
Issuance of Series A1 preferred stock at $1.55 per share in December 2001, in connection with merger	1,610,250	2,496	—	—	—	—	—	—	—	—	—	—
Issuance of Series B preferred stock for cash at $1.40 per share in December 2001, net of issuance costs of $71	6,441,000	8,946	—	—	—	—	—	—	—	—	—	—
Issuance of common stock in connection with merger at $1.10 per share in December 2001	—	—	—	—	868,922	—	956	—	—	—	—	956
Warrants assumed in merger transaction	—	—	—	—	—	—	10	—	—	—	—	10
Issuance of common stock for cash at $0.22 per share upon exercise of options in December 2001	—	—	—	—	9,090	—	2	—	—	—	—	2
Compensation expense related to consultant stock options	—	—	—	—	—	—	3	—	—	—	—	3
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	—	—	(5,652)	(5,652)
Balance at December 31, 2001 (carried forward)	10,551,250	$12,433	—	$—	1,332,548	$—	$1,071	$—	$—	$—	$(5,652)	$(4,581)

See accompanying notes.

ALEXZA PHARMACEUTICALS, INC.
(a development stage company)

CONSOLIDATED STATEMENT OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT) — (Continued)

	Convertible Preferred Stock		Preferred Stock		Common Stock		Additional Paid-In Capital	Stockholder Note Receivable	Deferred Stock Compensation	Other Comprehensive (Loss) Income	Deficit Accumulated During the Development Stage	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount						
	(In thousands, except share and per share amounts)											
Balance at December 31, 2001 (brought forward)	10,551,250	$12,433	—	$—	1,332,548	$—	$1,071	$ —	$—	$—	$ (5,652)	$ (4,581)
Issuance of common stock for cash at $0.22 per share upon exercise of options in February 2002	—	—	—	—	10,606	—	3	—	—	—	—	3
Issuance of warrants to purchase Series B preferred stock in March 2002, in connection with equipment financing loan	—	27	—	—	—	—	—	—	—	—	—	—
Issuance of common stock for cash at $0.22 per share upon exercise of options in July 2002	—	—	—	—	2,180	—	—	—	—	—	—	—
Issuance of common stock to stockholder at $0.99 per share in exchange for promissory note in July 2002	—	—	—	—	53,156	—	53	(53)	—	—	—	—
Issuance of Series C preferred stock for cash at $1.56 per share in September 2002, net of issuance costs of $108	28,870,005	44,892	—	—	—	—	—	—	—	—	—	—
Repurchase of common stock for cash at $1.05 per share in October 2002	—	—	—	—	(2,634)	—	(3)	—	—	—	—	(3)
Issuance of common stock for cash at $1.05 per share for services upon exercise of warrants in December 2002	—	—	—	—	9,368	—	10	—	—	—	—	10
Compensation expense related to consultant stock options	—	—	—	—	—	—	10	—	—	—	—	10
Unrealized gain on investments	—	—	—	—	—	—	—	—	—	51	—	51
Net loss	—	—	—	—	—	—	—	—	—	—	(8,163)	(8,163)
Comprehensive loss	—	—	—	—	—	—	—	—	—	—	—	(8,112)
Balance at December 31, 2002 (carried forward)	39,421,255	$57,352	—	$—	1,405,224	$—	$1,144	$(53)	$—	$51	$(13,815)	$(12,673)

See accompanying notes.

ALEXZA PHARMACEUTICALS, INC.
(a development stage company)

CONSOLIDATED STATEMENT OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT) — (Continued)

	Convertible Preferred Stock		Preferred Stock		Common Stock		Additional Paid-In Capital	Stockholder Note Receivable	Deferred Stock Compensation	Other Comprehensive (Loss) Income	Deficit Accumulated During the Development Stage	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount						
	(In thousands, except share and per share amounts)											
Balance at December 31, 2002 (brought forward)	39,421,255	$57,352	—	$—	1,405,224	$—	$1,144	$(53)	$—	$ 51	$(13,815)	$(12,673)
Issuance of common stock for cash at $0.22, $0.99 and $1.10 per share upon exercise of options	—	—	—	—	74,903	—	47	—	—	—	—	47
Issuance of warrants to purchase Series C preferred stock in connection with equipment financing loan in January 2003	—	35	—	—	—	—	—	—	—	—	—	—
Issuance of warrants to purchase Series C preferred stock in connection with equipment financing loan in September 2003	—	27	—	—	—	—	—	—	—	—	—	—
Repurchase of common stock for cash at $1.05 per share in January 2003	—	—	—	—	(1,172)	—	(1)	—	—	—	—	(1)
Repurchase of common stock for cash at $0.22 per share in November 2003	—	—	—	—	(14,772)	—	(3)	—	—	—	—	(3)
Compensation expense related to consultant stock options	—	—	—	—	—	—	31	—	—	—	—	31
Deferred stock compensation expense related to modification of consultant stock option	—	—	—	—	—	—	1	—	(1)	—	—	—
Unrealized loss on investments	—	—	—	—	—	—	—	—	—	(55)	—	(55)
Net loss	—	—	—	—	—	—	—	—	—	—	(14,328)	(14,328)
Comprehensive loss	—	—	—	—	—	—	—	—	—	—	—	(14,383)
Balance at December 31, 2003 (carried forward)	39,421,255	$57,414	—	$—	1,464,183	$—	$1,219	$(53)	$(1)	$ (4)	$(28,143)	$(26,982)

See accompanying notes.

ALEXZA PHARMACEUTICALS, INC.
(a development stage company)

CONSOLIDATED STATEMENT OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT) — (Continued)

	Convertible Preferred Stock		Preferred Stock		Common Stock		Additional Paid-In Capital	Stockholder Note Receivable	Deferred Stock Compensation	Other Comprehensive (Loss) Income	Deficit Accumulated During the Development Stage	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount						
	(In thousands, except share and per share amounts)											
Balance at December 31, 2003 (brought forward)	39,421,255	$ 57,414	—	$—	1,464,183	$—	$1,219	$(53)	$ (1)	$ (4)	$(28,143)	$(26,982)
Cancellation of unvested common stock at $0.99 per share in March 2004	—	—	—	—	(24,365)	—	(24)	24	—	—	—	—
Repayment of vested portion of stockholder note receivable for cash	—	—	—	—	—	—	—	29	—	—	—	29
Issuance of warrants to purchase Series C preferred stock in connection with equipment financing loan in April 2004	—	20	—	—	—	—	—	—	—	—	—	—
Issuance of common stock for cash at $0.22, $0.99 and $1.10 per share upon exercise of options	—	—	—	—	100,192	—	72	—	—	—	—	72
Repurchase of common stock for cash at $1.05 per share in September 2004	—	—	—	—	(404)	—	—	—	—	—	—	—
Issuance of Series D preferred stock at $1.29 per share in November and December 2004, net of issuance costs of $2,239	40,435,448	49,760	—	—	—	—	—	—	—	—	—	—
Issuance of warrants to purchase common stock in connection with Series D financing in November 2004	—	—	—	—	—	—	91	—	—	—	—	91
Compensation expense related to consultant stock options	—	—	—	—	—	—	40	—	—	—	—	40
Compensation expense related to employee stock option modifications	—	—	—	—	—	—	19	—	—	—	—	19
Amortization of deferred stock compensation	—	—	—	—	—	—	—	—	1	—	—	1
Unrealized loss on investments	—	—	—	—	—	—	—	—	—	(41)	—	(41)
Net loss	—	—	—	—	—	—	—	—	—	—	(16,625)	(16,625)
Comprehensive loss	—	—	—	—	—	—	—	—	—	—	—	(16,666)
Balance at December 31, 2004 (carried forward)	79,856,703	$107,194	—	$—	1,539,606	$—	$1,417	$ —	$—	$(45)	$(44,768)	$(43,396)

See accompanying notes.

ALEXZA PHARMACEUTICALS, INC.
(a development stage company)

CONSOLIDATED STATEMENT OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT) — (Continued)

	Convertible Preferred Stock		Preferred Stock		Common Stock		Additional Paid-In Capital	Stockholder Note Receivable	Deferred Stock Compensation	Other Comprehensive (Loss) Income	Deficit Accumulated During the Development Stage	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount						
	(In thousands, except share and per share amounts)											
Balance at December 31, 2004 (brought forward)	79,856,703	$107,194	—	$—	1,539,606	$—	$1,417	$—	$ —	$(45)	$(44,768)	$(43,396)
Issuance of common stock upon exercise of options $0.22, $0.99, $1.10, per share	—	—	—	—	380,508	—	357	—	—	—	—	357
Compensation expense related to consultant stock options	—	—	—	—	—	—	195	—	—	—	—	195
Deferred stock compensation, net of $4 reversal in connection with employee terminations	—	—	—	—	—	—	3,329	—	(3,329)	—	—	—
Amortization of deferred stock compensation,	—	—	—	—	—	—	—	—	404	—	—	404
Variable compensation expense	—	—	—	—	—	—	442	—	—	—	—	442
Unrealized gain on investments	—	—	—	—	—	—	—	—	—	15	—	15
Net loss	—	—	—	—	—	—	—	—	—	—	(32,402)	(32,402)
Comprehensive loss	—	—	—	—	—	—	—	—	—	—	—	(32,387)
Balance at December 31, 2005 (carried forward)	79,856,703	$107,194	—	$—	1,920,114	$—	$5,740	$—	$(2,925)	$(30)	$(77,170)	$(74,385)

See accompanying notes.

ALEXZA PHARMACEUTICALS, INC.
(a development stage company)

CONSOLIDATED STATEMENT OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT) — (Continued)

	Convertible Preferred Stock		Preferred Stock		Common Stock		Additional Paid-In Capital	Stockholder Note Receivable	Deferred Stock Compensation	Other Comprehensive (Loss) Income	Deficit Accumulated During the Development Stage	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount						
	(In thousands, except share and per share amounts)											
Balance at December 31, 2005 (brought forward)	79,856,703	$ 107,194	—	$—	1,920,114	$—	$ 5,740	$—	$(2,925)	$(30)	$ (77,170)	$ (74,385)
Issuance of common stock for cash and shares upon exercise of options at a weighted average price of $1.28 per share	—	—	—	—	159,446	—	195	—	—	—	—	195
Issuance of common stock for cash under the Company's Employee Stock Purchase Plan	—	—	—	—	131,682	—	896	—	—	—	—	896
Issuance of common stock for shares upon exercise of warrant	—	—	—	—	85,359	—	—	—	—	—	—	—
Issuance of common stock for cash, net of offering costs of $2,156	—	—	—	—	6,325,000	1	44,901	—	—	—	—	44,902
Conversion of convertible preferred stock into common stock	(79,856,703)	(107,194)	—	—	15,197,712	1	107,193	—	—	—	—	107,194
Compensation expense related to consultant stock options	—	—	—	—	—	—	145	—	—	—	—	145
Compensation expense related to fair value of employee share based awards issued after January 1, 2006	—	—	—	—	—	—	1,601	—	—	—	—	1,601
Amortization of deferred stock compensation	—	—	—	—	—	—	—	—	727	—	—	727
Reversal of deferred stock compensation in connection with employee terminations	—	—	—	—	—	—	(495)	—	495	—	—	—
Variable compensation expense	—	—	—	—	—	—	(442)	—	—	—	—	(442)
Issuance of warrant to Symphony Allegro Holdings LLC		—	—	—	—	—	10,708	—	—	—	—	10,708
Unrealized gain on investments	—	—	—	—	—	—	—	—	—	39	—	39
Net loss	—	—	—	—	—	—	—	—	—	—	(41,806)	(41,806)
Comprehensive loss	—	—	—	—	—	—	—	—	—	—	—	(41,767)
Balance at December 31, 2006 (carried forward)	—	$ —	—	$—	23,819,319	$ 2	$170,442	$—	$(1,703)	$ 9	$(118,976)	$ 49,774

See accompanying notes.

ALEXZA PHARMACEUTICALS, INC.
(a development stage company)

CONSOLIDATED STATEMENT OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT) — (Continued)

	Convertible Preferred Stock		Preferred Stock		Common Stock		Additional Paid-In Capital	Stockholder Note Receivable	Deferred Stock Compensation	Other Comprehensive (Loss) Income	Deficit Accumulated During the Development Stage	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount						
	(In thousands, except share and per share amounts)											
Balance at December 31, 2006 (brought forward)	—	$—	—	$—	23,819,319	$ 2	$170,442	$—	$(1,703)	$ 9	$(118,976)	$ 49,774
Issuance of common stock for cash and shares upon exercise of options at a weighted average price of $1.28 per share	—	—	—	—	204,423	—	432	—	—	—	—	432
Issuance of common stock for cash under the Company's Employee Stock Purchase Plan	—	—	—	—	205,870	—	1,405	—	—	—	—	1,405
Issuance of common stock upon vesting of restricted stock units	—	—	—	—	8,245	—	—	—	—	—	—	—
Issuance of common stock for cash, net of offering costs of $4,743	—	—	—	—	6,900,000	1	65,981	—	—	—	—	65,982
Compensation expense related to consultant stock options	—	—	—	—	—	—	75	—	—	—	—	75
Compensation expense related to fair value of employee share based awards issued after January 1, 2006	—	—	—	—	—	—	2,733	—	—	—	—	2,733
Amortization of deferred stock compensation	—	—	—	—	—	—	—	—	577	—	—	577
Reversal of deferred stock compensation in connection with employee terminations	—	—	—	—	—	—	(387)	—	387	—	—	—
Unrealized gain on investments	—	—	—	—	—	—	—	—	—	132	—	132
Net loss	—	—	—	—	—	—	—	—	—	—	(45,119)	(45,119)
Comprehensive loss	—	—	—	—	—	—	—	—	—	—	—	(44,987)
Balance at December 31, 2007(carried forward)	—	$—	—	$—	31,137,857	$ 3	$240,681	$—	$ (739)	$141	$(164,095)	$ 75,991

See accompanying notes.

ALEXZA PHARMACEUTICALS, INC.
(a development stage company)

	Convertible Preferred Stock		Preferred Stock		Common Stock		Additional Paid-In Capital	Stockholder Note Receivable	Deferred Stock Compensation	Other Comprehensive (Loss) Income	Deficit Accumulated During the Development Stage	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount						
	(In thousands, except share and per share amounts)											
Balance at December 31, 2007 (brought forward)	—	$—	—	$—	31,137,857	$ 3	$240,681	$—	$(739)	$ 141	$(164,095)	$ 75,991
Issuance of common stock and common stock warrant for cash	—	—	—	—	1,250,000	—	9,840	—	—	—	—	9,840
Issuance of common stock for cash and shares upon exercise of options at a weighted average price of $1.55 per share	—	—	—	—	104,428	—	161	—	—	—	—	161
Issuance of common stock for cash under the Company's Employee Stock Purchase Plan	—	—	—	—	305,146	—	1,172	—	—	—	—	1,172
Issuance of common stock upon vesting of restricted stock units	—	—	—	—	23,443	—	—	—	—	—	—	—
Compensation expense related to consultant stock options	—	—	—	—	—	—	22	—	—	—	—	22
Compensation expense related to fair value of employee share based awards issued after January 1, 2006	—	—	—	—	—	—	4,633	—	—	—	—	4,633
Amortization of deferred stock compensation	—	—	—	—	—	—	—	—	437	—	—	437
Reversal of deferred stock compensation in connection with employee terminations	—	—	—	—	—	—	(83)	—	83	—	—	—
Unrealized loss on investments	—	—	—	—	—	—	—	—	—	(113)	—	(113)
Net loss	—	—	—	—	—	—	—	—	—	—	(58,450)	(58,450)
Comprehensive loss	—	—	—	—	—	—	—	—	—	—	—	(58,563)
Balance at December 31, 2008	—	$—	—	$—	32,820,874	$ 3	$256,426	$—	$(219)	$ 28	$(222,545)	$ 33,693

See accompanying notes.

ALEXZA PHARMACEUTICALS, INC
(a development stage company)

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year Ended December 31,			Period from December 19, 2000 (Inception) to December 31, 2008
	2008	2007	2006	
	(In thousands)			
Cash flows from operating activities:				
Net loss	$(58,450)	$(45,119)	$(41,806)	$(222,545)
Adjustments to reconcile net loss to net cash used in operating activities:				
Loss attributed to noncontrolling interests	(18,591)	(10,791)	(1,720)	(31,102)
Share-based compensation expense	5,092	3,385	2,217	11,839
Extinguishment of officer note receivable	—	—	—	2,300
Issuance of common stock for intellectual property	—	—	—	92
Charge for acquired in-process research and development	—	—	—	3,916
Amortization of assembled workforce	—	—	—	222
Amortization of debt discount and deferred interest	38	49	35	362
Amortization of discount on available-for-sale securities	(797)	(929)	(1,035)	(727)
Depreciation	5,294	4,016	3,677	16,759
Loss on disposal of property and equipment	17	23	28	83
Changes in operating assets and liabilities:				
Receivables	12,055	(12,055)	35	—
Prepaid expenses and other current assets	247	(114)	534	(1,124)
Other assets	(24)	42	7	(2,625)
Accounts payable	(278)	(727)	3,009	4,799
Accrued clinical trial expense and other accrued liabilities	111	898	505	2,799
Deferred revenues	(486)	10,000	—	9,514
Other liabilities	701	15,494	1,191	20,776
Net cash used in operating activities	(55,071)	(35,828)	(33,323)	(184,662)
Cash flows from investing activities:				
Purchase of available-for-sale securities	(47,111)	(62,466)	(72,129)	(324,913)
Maturities of available-for-sale securities	74,329	51,064	69,194	314,149
Purchase of available-for-sale securities held by Symphony Allegro, Inc.	—	—	(49,975)	(49,975)
Maturities of available-for-sale securities held by Symphony Allegro, Inc.	18,131	10,507	19	28,657
Decrease (increase) in restricted cash	204	—	(400)	(400)
Purchases of property and equipment	(2,732)	(19,059)	(8,067)	(40,157)
Proceeds from disposal of property and equipment	25	—	—	28
Cash paid for merger	—	—	—	(250)
Net cash provided by (used in) investing activities	42,846	(19,954)	(61,358)	(72,861)
Cash flows from financing activities:				
Proceeds from issuance of common stock and exercise of stock options and stock purchase rights	11,173	67,819	45,993	125,485
Repurchase of common stock	—	—	—	(8)
Proceeds from issuance of convertible preferred stock	—	—	—	104,681
Proceeds from repayment of stockholder note receivable	—	—	—	29
Proceeds from equipment term loans	—	5,814	3,997	18,932
Payments of equipment term loans and leases	(4,249)	(3,546)	(2,235)	(12,731)
Proceeds from purchase of non controlling interest by preferred shareholders in Symphony Allegro, Inc., net of fees	—	—	47,171	47,171
Net cash provided by financing activities	6,924	70,087	94,926	283,559
Net increase (decrease) in cash and cash equivalents	(5,301)	14,305	245	26,036
Cash and cash equivalents at beginning of period	31,337	17,032	16,787	—
Cash and cash equivalents at end of period	$ 26,036	$ 31,337	$ 17,032	$ 26,036
Supplemental disclosures of cash flow information				
Cash paid for interest	$ 935	$ 1,003	$ 728	$ 3,265
Non cash investing and financing activities:				
Conversion of convertible preferred stock to common stock	$ —	$ —	$107,194	$ 107,194
Warrant issued in conjunction with Symphony Allegro transaction	$ —	$ —	$ 10,708	$ 10,708

See accompanying notes.

1. The Company and Basis of Presentation

Business

Alexza Pharmaceuticals, Inc. ("Alexza" or the "Company"), was incorporated in the state of Delaware on December 19, 2000 as FaxMed, Inc. In June 2001, the Company changed its name to Alexza Corporation and in December 2001 became Alexza Molecular Delivery Corporation. In July 2005, the Company changed its name to Alexza Pharmaceuticals, Inc.

The Company is a pharmaceutical development company focused on the research, development, and commercialization of novel proprietary products for the acute treatment of central nervous system ("CNS") conditions. The Company's primary activities since incorporation have been establishing its offices, recruiting personnel, conducting research and development, conducting preclinical studies and clinical trials, performing business and financial planning, and raising capital. Accordingly, the Company is considered to be in the development stage and operates in one business segment.

Basis of Consolidation

The consolidated financial statements include the accounts of Alexza, its wholly-owned subsidiaries, Alexza Singapore Pte. Ltd., ("ASPL"), Alexza Singapore Manufacturing Pte. Ltd., and Alexza UK, Limited, and Alexza's variable interest entity, Symphony Allegro, Inc. ("Allegro"). Alexza is considered the primary beneficiary of Allegro as defined in Financial Accounting Standards Board ("FASB") Interpretation No. 46 (revised 2003), *Consolidation of Variable Interest Entities* ("FIN 46R"). All significant intercompany balances and transactions have been eliminated.

Public Offerings

In March 2006, the Company completed its initial public offering of 6,325,000 shares of its common stock, including the full underwriters' over-allotment option, at a public offering price of $8.00 per share. Net cash proceeds from the initial public offering were approximately $44.9 million, after deducting underwriting discounts and commissions and other offering expenses. In connection with the closing of the initial public offering, all of the Company's shares of convertible preferred stock outstanding at the time of the offering were automatically converted into 15,197,712 shares of common stock.

In May 2007, the Company completed a public offering of 6,900,000 shares of its common stock, including the full underwriters' over-allotment option, at a public offering price of $10.25 per share. Net cash proceeds from the public offering were approximately $66.0 million, after deducting underwriting discounts and commissions and other offering expenses

Equity Financing Facility

In March 2008, the Company obtained a committed equity line of credit under which the Company may sell, subject to certain limitations, up to $50 million of its registered common stock to Azimuth Opportunity, Ltd. ("Azimuth") over a 24-month period. The Company is not obligated to utilize any of the $50 million equity line of credit.

The Company will determine, at its sole discretion, the timing, the dollar amount, and the minimum price per share of each draw under this equity line of credit, subject to certain conditions. When and if the Company elects to use the equity line of credit, the Company will issue shares to Azimuth at a discount of between 4.15% and 6.00% to the volume weighted average price of the Company's common stock over a preceding period of trading days. Azimuth is not required to purchase any shares below $5.00 per share, and any shares sold under this equity line of credit will be sold pursuant to a shelf registration statement declared effective by the SEC on April 16, 2007. The

agreement will terminate on March 31, 2010. As of December 31, 2008, there have been no sales of common stock under this agreement.

Registered Direct Equity Issuance

In March 2008, the Company completed the sale of 1,250,000 shares of its registered common stock to Biomedical Sciences Investment Fund Pte. Ltd. ("Bio*One") at a price of $8.00 per share. As outlined in the agreement, if the average closing price of the Company's stock over a 45 consecutive day trading period does not exceed $8.00 between the closing date and December 31, 2008, Bio*One would receive 135,041 additional shares, which would adjust the effective purchase price to $7.22 per share. The Company's average stock price did not meet this level during the specified period and the Company issued the additional shares to Bio*One in January 2009.

In addition, the Company issued a warrant to Bio*One to purchase up to 375,000 of additional shares of Alexza common stock at a purchase price per share of $8.00. The warrant was subject to the same price adjustment as the common stock sale, and effective January 1, 2009 the warrant was automatically adjusted to give Bio*One the right to purchase 415,522 shares at a purchase price of $7.22 per share. The Company committed to initiate and maintain manufacturing operations in Singapore, and the warrant was to become exercisable only if the Company terminated operations in Singapore or did not achieve certain performance milestones. In December 2008, the Company did not meet its defined performance milestone, and as a result the warrant became fully exercisable. The warrant has a maximum term of 5 years.

All securities sold to Bio*One were sold pursuant to a shelf registration statement declared effective by the SEC on April 16, 2007. Net proceeds from the sale of the stock and warrant were approximately $9.84 million after deducting offering expenses.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates.

Significant Risks and Uncertainties

The Company has incurred significant losses from operations since its inception and expects losses to continue for the foreseeable future. The Company has financed its operations primarily through the sale of equity securities, licensing collaborations, capital lease and equipment financing and government grants. The Company will need to raise additional capital to fund its operations, to develop its product candidates, to develop its manufacturing capabilities, and to reacquire program rights currently licensed to Symphony Allegro, Inc. (see note 8), and such funding may not be available or may be on terms which are not favorable to the Company.

Fair Value of Financial Instruments

The Company carries cash, cash equivalents and available for sale marketable securities at fair value. The Company's other financial instruments, including accounts payable and accrued liabilities, are carried at cost, which management believes approximates fair value given their short-term nature.

Effective January 1, 2008, the Company adopted Statement of Financial Accounting Standard No. 157, *Fair Value Measurements* ("SFAS 157"). SFAS 157 defines fair value, establishes a framework for measuring fair value in accordance with generally accepted accounting principles, and enhances disclosures about fair value measurements. The Company applies the provisions of SFAS 157 prospectively. Fair value is defined under SFAS 157 as the

exchange price that would be received for an asset or paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value under SFAS 157 must maximize the use of observable inputs and minimize the use of unobservable inputs. The standard describes a fair value hierarchy based on three levels of inputs, of which the first two are considered observable and the last unobservable, that may be used to measure fair value which are the following:

- *Level 1* — Quoted prices in active markets for identical assets or liabilities.
- *Level 2* — Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.
- *Level 3* — Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

In February 2008, the FASB issued FASB Staff Position 157-2 *Partial Deferral of the Effective Date of Statement 157* ("FSP 157-2"). FSP 157-2 delays the effective date of SFAS 157 for nonfinancial assets and nonfinancial liabilities, except for items that are recognized or disclosed at fair value in the financial statements on a recurring basis, at least annually, to fiscal years beginning after November 15, 2008.

In accordance with FSP 157-2, we deferred the adoption of SFAS 157 for one year for nonfinancial assets and nonfinancial liabilities that are recognized or disclosed at fair value in the financial statements on a nonrecurring basis. The adoption of SFAS 157 for financial assets and financial liabilities, effective January 1, 2008, did not have a material effect on the Company's consolidated financial position, operating results or cash flows.

Fair values of cash equivalents and marketable securities approximate book value primarily due to the short-term maturities of the investments and the low incidence of changes in security credit ratings. Unrealized gains on available-for-sale securities of $28,000 were reported as a component of stockholders' equity.

The following table represents the Company's fair value hierarchy, as defined by SFAS 157, for its financial assets (cash equivalents and marketable securities and investments held by Symphony Allegro, Inc.) measured at fair value on a recurring basis as of December 31, 2008 (in thousands):

	Level 1	Level 2	Level 3	Total
Money market funds	$19,350	$ —	$—	$19,350
Money market fund held by Symphony Allegro, Inc.	21,318	—	—	21,318
Corporate debt securities	—	9,649	—	9,649
Government securities	—	1,505	—	1,505
Government-sponsored enterprises	—	6,620	—	6,620
Total	$40,668	$17,774	$—	$58,442

The marketable securities held by Symphony Allegro are used to fund the development of AZ-002, AZ-004 and AZ-104 and are not available for general corporate expenses.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to credit risk consist of cash, cash equivalents and marketable securities and restricted cash to the extent of the amounts recorded on the balance sheets. The Company's cash, cash equivalents, marketable securities and restricted cash are placed with high credit-quality U.S. financial institutions and issuers. All cash, cash equivalents, marketable securities and investments held by Symphony Allegro, Inc. are maintained with financial institutions that the Company's management believes are

high credit-quality. Marketable securities held by Symphony Allegro, Inc. consist of investments in a money market fund that invests primarily in domestic commercial paper, securities issued or guaranteed by the U.S. government or its agencies, U.S. and Yankee bank obligations and fully collateralized repurchase agreements. The Company believes that its established guidelines for investment of its excess cash maintain liquidity through its policies on diversification and investment maturity.

Cash Equivalents and Marketable Securities

Management determines the appropriate classification of its investments at the time of purchase. These securities are recorded as either cash equivalents or marketable securities.

The Company considers all highly liquid investments with original maturities of three months or less from date of purchase to be cash equivalents. Cash equivalents consist of interest-bearing instruments including obligations of U.S. government agencies, high credit rating corporate borrowers and money market funds, which are carried at market value.

All other investments are classified as available-for-sale marketable securities. The Company views its available-for-sale investments as available for use in current operations. Accordingly, the Company has classified all investments as short-term marketable securities, even though the stated maturity date may be one year or more beyond the current balance sheet date. Marketable securities are carried at estimated fair value with unrealized gains or losses included in accumulated other comprehensive income (loss) in stockholders' equity.

The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion are included in interest and other income (expense), net. Realized gains and losses, if any, are also included in interest and other income (expense), net. The cost of all securities sold is based on the specific-identification method. Interest and dividends are included in interest income.

The Company reviews its investments for other than temporary decreases in market value on a quarterly basis. Through December 31, 2008, the Company has not recorded an other than temporary impairment.

Property and Equipment

Property and equipment are stated at cost, less accumulated depreciation. Property and equipment are depreciated using the straight-line method over the estimated life of the asset, generally three years for computer equipment and five years for laboratory equipment and furniture. Leasehold improvements are amortized over the estimated useful life or the remaining lease term, whichever is shorter.

Restricted Cash

Under the Company's facility lease agreements and an agreement with its utilities provider, the Company must maintain letters of credit as security for performance under these agreements. The letters of credit are secured by certificates of deposits in amounts equal to the letters of credit, which are classified as restricted cash, a non-current asset. At December 31, 2008 and 2007 the Company maintained the following letters of credit and restricted cash balances (in thousands):

	December 31,	
	2008	2007
Mt. View facility	$400	$400
Palo Alto facilities	—	163
Palo Alto utility account	—	41
	$400	$604

Impairment of Long-Lived Assets

The Company reviews long-lived assets, including property and equipment, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition are less than its carrying amount. The impairment loss, if recognized, would be based on the excess of the carrying value of the impaired asset over its respective fair value. Impairment, if any, is assessed using discounted cash flows. Through December 31, 2008, the Company has not recorded an impairment of a long-lived asset.

Revenue Recognition

The Company recognizes revenue in accordance with the Securities and Exchange Commission ("SEC") Staff Accounting Bulletin ("SAB") No. 101, *Revenue Recognition in Financial* Statements ("SAB 101"), as amended by Staff Accounting Bulletin No. 104, *Revision of Topic 13* ("SAB 104").

Revenue has consisted primarily of amounts earned under research grants with the National Institutes of Health and from the Endo licensing agreement. The Company's federal government research grants provided for the reimbursement of qualified expenses for research and development as defined under the terms of each grant. Equipment purchased specifically for grant programs was recorded at cost and depreciated over the grant period. Revenue under grants was recognized when the related qualified research and development expenses were incurred up to the limit of the approval funding amounts.

In determining the accounting for collaboration agreements such as the Endo licensing agreement, see Note 8, the Company follows the provisions of Emerging Issues Task Force ("EITF") Issue 00-21, *Revenue Arrangements with Multiple Deliverables* ("EITF 00-21"). EITF 00-21 provides guidance on whether an arrangement involves multiple revenue-generating deliverables that should be accounted for as a single unit of accounting or divided into separate units of accounting for revenue recognition purposes and, if this division is required, how the arrangement consideration should be allocated among the separate units of accounting. If the arrangement represents a single unit of accounting, the revenue recognition policy and the performance obligation period must be determined, if not already contractually defined, for the entire arrangement. If the arrangement represents separate units of accounting according to the EITF's separation criteria, a revenue recognition policy must be determined for each unit. Revenues for non-refundable upfront license fee payments, where the Company continues to have obligations, will be recognized as performance occurs and obligations are completed.

Research and Development

Research and development expenses include personnel and facility-related expenses, outside contracted services including clinical trial costs, manufacturing and process development costs, research costs and other consulting services. Research and development costs are expensed as incurred.

Clinical development costs are a significant component of research and development expenses. The Company has a history of contracting with third parties that perform various clinical trial activities on its behalf in the ongoing development of its product candidates. The financial terms of these contracts are subject to negotiations and may vary from contract to contract and may result in uneven payment flow. The Company accrues and expenses costs for clinical trial activities performed by third parties based upon estimates of the percentage of work completed over the life of the individual study in accordance with agreements established with contract research organizations and clinical trial sites.

Income Taxes

The Company utilizes the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on differences between financial reporting and tax basis of assets and liabilities and are measured using enacted tax rates and laws that will be in effect when the differences are expected to reverse. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized.

In July 2006, FASB issued Interpretation No. 48, *Accounting for Uncertainty in Income Taxes — An Interpretation of FASB Statement No. 109* ("FIN 48"). FIN 48 clarifies the accounting for uncertainty in income taxes recognized in an entity's financial statements in accordance with FASB Statement No. 109, *Accounting for Income Taxes* and prescribes a recognition threshold and measurement attributes for financial statement disclosure of tax positions taken or expected to be taken on a tax return. Under FIN 48, the impact of an uncertain income tax position on the income tax return must be recognized at the largest amount that is more-likely-than-not to be sustained upon audit by the relevant taxing authority. An uncertain income tax position will not be recognized if it has less than a 50% likelihood of being sustained. Additionally, FIN 48 provides guidance on de-recognition, classification, interest and penalties, accounting in interim periods, disclosure and transition.

The Company adopted the accounting policy that interest recognized in accordance with Paragraph 15 of FIN 48 and penalties recognized in accordance with Paragraph 16 of FIN 48 are classified as part of its income tax provision.

Comprehensive Income (Loss)

Comprehensive income (loss) is comprised of net loss and unrealized gains (losses) on marketable securities. Total comprehensive income (loss) for all periods presented has been disclosed in the Company's Consolidated Statement of Convertible Preferred Stock and Stockholders' Equity (Deficit).

Share-Based Compensation

In December 2004, the FASB issued Statement of Financial Accounting Standards 123R ("SFAS 123R"), *Share-Based Payment.* This revised standard addresses the accounting for share-based payment transactions in which a company receives employee services in exchange for either equity instruments of the company or liabilities that are based on the fair value of the company's equity instruments or that may be settled by the issuance of such equity instruments. Under SFAS 123R, companies are no longer able to account for share-based compensation transactions using the intrinsic-value method, the Company's previous accounting method, in accordance with Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees* ("APB 25"). Instead, companies are required to account for such transactions using a fair-value method and recognize the expense in the statement of operations.

On January 1, 2006, the Company adopted SFAS 123R using the prospective transition method, as required by the statement. Under this transition method, beginning January 1, 2006, employee share-based compensation cost recognized includes: (a) compensation cost for all share-based payments granted prior to, but not yet vested, as of December 31, 2005 for (i) employees using the intrinsic value in accordance with the provisions of APB 25 and (ii) non-employees using the fair value in accordance with the provisions of SFAS 123, and (b) compensation cost for all share-based payments granted or modified subsequent to December 31, 2005, based on the fair value estimated in accordance with the provisions of SFAS 123R.

All share-based payment awards are amortized on a ratable basis over the requisite service periods of the awards, which are generally the vesting periods. There was no share-based compensation capitalized as of December 31, 2008.

Employee Share-Based Awards Granted Prior to January 1, 2006

Compensation cost for employee stock options granted prior to January 1, 2006, the date the Company adopted SFAS 123R, are accounted for using the option's intrinsic value. The Company recorded the total valuation of these options as a component of stockholders' equity (deficit), which will be amortized over the vesting period of the applicable option on a straight line basis. During the years ended December 31, 2008, 2007 and 2006, the Company reversed $83,000, $387,000 and $495,000, respectively, of deferred stock-based compensation related to unvested options cancelled as a result of employee terminations. The remaining deferred stock compensation balance of $219,000 will be amortized in 2009.

Employee Share-Based Awards Granted On or Subsequent to January 1, 2006

Compensation cost for employee share-based awards granted on or after January 1, 2006, the date the Company adopted SFAS 123R, is based on the grant-date fair value estimated in accordance with the provisions of SFAS 123R and will be recognized over the vesting period of the applicable award on a straight-line basis. The Company issues employee share-based awards in the form of stock options and restricted stock units under the Company's equity incentive plans and stock purchase rights under the Company's employee stock purchase plan.

Stock Options, Stock Purchase Rights and Restricted Stock Units

During the years ended December 31, 2008, 2007 and 2006, the weighted average fair value of the employee stock options granted was $3.04, $6.22 and $5.50, respectively, the weighted average fair value of stock purchase rights granted was $2.58, $3.44 and $3.23, respectively, and the weighted average fair value of restricted stock units granted was $4.35, $8.89 and $7.00, respectively.

The estimated grant date fair values of the stock options and stock purchase rights were calculated using the Black-Scholes valuation model, and the following assumptions:

	Year Ended December 31,		
	2008	2007	2006
Stock Option Plans			
Weighted-average expected term	5.0 years	6.1 years	6.1 years
Expected volatility	67%	73%	80%
Risk-free interest rate	3.14%	4.72%	4.71%
Dividend yield	0%	0%	0%
Employee Stock Purchase Plan			
Weighted-average expected term	1.65 years	1.42 years	1.4 years
Expected volatility	71%	53%	53%
Risk-free interest rate	2.68%	4.31%	4.77%
Dividend yield	0%	0%	0%

Weighted-Average Expected Life Prior to January 1, 2008, the expected term of options granted was determined using the "shortcut" method, as illustrated in the Securities and Exchange Commission's Staff Accounting Bulletin No. 107 ("SAB 107"). Under this approach, the expected term was presumed to be the average of the vesting term and the contractual term of the option. As detailed information about the employees' exercise behavior is now available to the Company, beginning on January 1, 2008, the Company no longer uses the above mentioned shortcut method and determines the expected term of the options granted through a combination of the Company's own historical exercise experience and expected future exercise activities and post-vesting termination behavior. The change of approach in determining the estimated weighted average expected life resulted in the assumption decreasing from approximately 6.1 years to 5.0 years.

Under the Employee Stock Purchase Plan, the expected term of employee stock purchase plan shares is the average of the purchase periods under each offering period.

Volatility Prior to January 1, 2008, as the Company considered itself a newly public entity with insufficient historical data on volatility of its stock, the expected volatility used was based on volatility of similar entities (referred to as "guideline" companies). In evaluating similarity, the Company considered factors such as industry, stage of life cycle and size. Due to the availability of historical volatility data of the Company's own stock, the Company began utilizing its historical volatility to determine future volatility for the purpose of determining share-based payments for all options granted on or after January 1, 2008.

Risk-Free Interest Rate. The risk-free rate that the Company uses in the Black-Scholes option valuation model is based on U.S. Treasury zero-coupon issues with remaining terms similar to the expected term of the options or purchase rights on the respective grant dates.

Dividend Yield The Company has never declared or paid any cash dividends and does not plan to pay cash dividends in the foreseeable future, and, therefore, used an expected dividend yield of zero in the valuation model.

Forfeiture Rate The Company uses historical data to estimate pre-vesting option forfeitures and record stock-based compensation expense only for those awards that are expected to vest. All stock-based payment awards are amortized on a straight-line basis over the requisite service periods of the awards, which are generally the vesting periods. The Company increased its estimated forfeiture rate during the three months ended March 31, 2008 from approximately 5.9% at December 31, 2007 to approximately 7.0%.

Restricted Stock Units The estimated fair value of restricted stock units awards is calculated based on the market price of Alexza's common stock on the date of grant, reduced by the present value of dividends expected to be paid on Alexza common stock prior to vesting of the restricted stock unit. The Company's estimate assumes no dividends will be paid prior to the vesting of the restricted stock unit.

As of December 31, 2008, there was $7,880,000, $813,000 and $1,228,000 total unrecognized compensation costs related to non-vested stock option awards issued after January 1, 2006, non-vested restricted stock units and stock purchase rights, respectively, which are expected to be recognized over a weighted average period of 2.5 years, 2.9 years and 1.4 years, respectively.

Settlement and Modification of Stock Option Awards

On March 7, 2006 ("the Settlement Date"), in settlement for the extinguishment of certain housing loans to three Company officers (see Note 9), the Company increased the exercise price on certain stock option awards held by these officers from $1.10 per share to $8.00 per share, which reduced the aggregate intrinsic value of these options by $3.4 million. These options were accounted for as variable awards. As a result of changes in the Company's stock price, the Company recorded a $442,000 reduction in share-based compensation expense during the three months ended March 31, 2006. As the exercise price was fixed in March 2006, the contingency was resolved and variable accounting for these options ceased.

Also on the Settlement Date, the Company entered into amended loan extinguishment agreements with the above mentioned officers, whereby the Company was given the right to increase the exercise price of selected options to $8.00 per share, resulting in an additional reduction in aggregate intrinsic value of $0.6 million. This modification was accounted for under SFAS 123R, and resulted in no additional share-based compensation expense.

Recent Accounting Pronouncements

Statement of Financial Accounting Standard No. 141R

In December 2007, the FASB issued Statement of Financial Accounting Standard No. 141 (revised 2007), *Business Combinations* ("SFAS 141(R)"). This standard establishes principles and requirements for how an acquirer in a business combination recognizes and measures the identifiable assets acquired, the liabilities assumed and any noncontrolling interest in the acquiree in its financial statements. SFAS 141(R) also establishes principles and requirements for how an acquirer recognizes and measures the goodwill acquired in a business combination and it establishes disclosure requirements to facilitate an evaluation of the nature and financial effects of a business combination. SFAS 141(R) is effective for business combinations which occur during the first annual reporting period beginning on or after December 15, 2008. The Company expects the effect of adoption of this standard will be limited to any acquisitions made by the Company which close subsequent to December 31, 2008.

Statement of Financial Accounting Standard No. 160

In December 2007, the FASB issued Statement of Financial Accounting Standard No. 160, *Noncontrolling Interests in Consolidated Financial Statements — An Amendment of ARB No. 51* ("SFAS 160"). SFAS 160 will require that noncontrolling interests in subsidiaries be reported as a component of stockholders' equity in the consolidated balance sheet. SFAS 160 also requires that earnings or losses attributed to the noncontrolling interests be reported as part of consolidated earnings and not as a separate component of income or expense, as well as requires disclosure of the attribution of consolidated earnings to the controlling and noncontrolling interests on the face of the consolidated statement of operations. SFAS 160 is effective for fiscal years beginning after December 15, 2008. Beginning in the first quarter of 2009, the Company will adopt these reporting requirements.

Emerging Issues Task Force Issue No. 07-3

Effective January 1, 2008, the Company adopted the Emerging Issues Task Force Issue No. 07-3 ("EITF 07-3"), *Accounting for Nonrefundable Advance Payments for Goods or Services to Be Used in Future Research and Development Activities.* The scope of EITF 07-3 is limited to nonrefundable advance payments for goods and services to be used or rendered in future research and development activities pursuant to an executory contractual arrangement. This issue provides that nonrefundable advance payments for goods or services that will be used or rendered for future research and development activities should be deferred and capitalized. We adopted the provisions of EITF 07-3 prospectively for new contracts entered into on or after January 1, 2008. The adoption of the provisions of EITF 07-3 on January 1, 2008 did not have a material impact on the Company's financial position, results of operations or cash flows.

3. Net Loss per Share

Basic and diluted net loss per share is calculated by dividing the net loss by the weighted-average number of common shares outstanding for the period less weighted average shares subject to repurchase, of which there were none in 2008, 2007 or 2006. Outstanding stock options, warrants, unvested restricted stock units, and shares to be issued upon conversion of outstanding convertible preferred stock, if any, are not included in the net loss per share calculation for the years ended December 31, 2008, 2007 and 2006 because the inclusion of such shares would have had an anti-dilutive effect.

Potentially dilutive securities include the following (in thousands):

	Year Ended December 31,		
	2008	2007	2006
Outstanding stock options	4,183	3,207	2,611
Unvested restricted stock units	172	93	34
Warrants to purchase common stock	2,431	2,016	2,016
Convertible preferred stock	—	—	—

4. Cash, Cash Equivalents, Marketable Securities and Restricted Cash

Cash, cash equivalents, marketable securities and restricted cash consisted of:

	December 31,	
	2008	2007
	(In thousands)	
Cash	$ 432	$ 327
Money market accounts	19,350	17,527
Certificates of deposit	400	604
Government debt securities	1,505	—
Government-sponsored enterprise debt securities	6,620	5,998
Corporate debt securities	9,649	44,049
Asset-backed securities	—	1,490
	$37,956	$69,995
Reported as:		
Cash and cash equivalents	$26,036	$31,337
Marketable securities	11,520	38,054
Restricted cash	400	604
	$37,956	$69,995

At December 31, 2008, all securities had a maturity date of less than one year.

5. Property and Equipment

Property and equipment consisted of the following:

	December 31,	
	2008	2007
	(In thousands)	
Lab equipment	$ 12,038	$ 10,628
Computer equipment and software	4,885	4,763
Furniture	1,123	996
Leasehold improvements	19,135	20,687
	37,181	37,074
Less: accumulated depreciation	(13,029)	(10,918)
	$ 24,152	$ 26,156

Property and equipment also includes equipment that secures the Company's equipment financing agreements of $14,338,000 and $16,036,000 at December 31, 2008 and 2007, respectively. Accumulated depreciation related to assets under the equipment financing loans was $9,588,000 and $9,190,000 at December 31, 2008 and 2007, respectively. Depreciation of property and equipment under equipment financing agreements is included in depreciation expense in the statement of cash flows.

6. Other Accrued Liabilities

Other accrued liabilities consisted of the following:

	December 31,	
	2008	2007
	(In thousands)	
Accrued compensation	$4,012	$3,532
Accrued professional fees	439	555
Other	754	1,000
	$5,205	$5,087

7. Commitments

Equipment Financing Obligations

The Company finances a portion of its fixed asset acquisitions through equipment financing agreements. Loans drawn from the equipment financing agreement are secured by certain fixed assets of the Company. Fixed asset purchases used to secure draws on the equipment financing agreement are recorded on the Company's balance sheet at cost. A liability is recorded upon the Company making a draw on the agreements.

The loans are repaid in 36 — 48 monthly installments, from the date of each draw, of principal and interest. The interest rate, which is fixed for each draw, is based on the U.S. Treasuries of comparable maturities and ranges from 9.2% to 10.6%. The equipment purchased under the equipment financing agreement is pledged as security. As of December 2008, no additional borrowings were available under the agreements.

Future principal payments under the equipment financing agreements as of December 31, 2008 are as follows (in thousands):

2009	$4,139
2010	2,088
2011	427
Total	$6,654

Operating Leases

The Company leases two buildings with an aggregate of 106,894 square feet of manufacturing, office and laboratory facilities in Mountain View, California, which the Company began to occupy in the fourth quarter of 2007. The Company recognizes rental expense on the facility on a straight line basis over the initial term of the lease. Differences between the straight line rent expense and rent payments are classified as deferred rent liability on the balance sheet. The lease for both facilities expires on March 31, 2018, and the Company has two options to extend the lease for five years each.

The Mountain View lease, as amended, included $15,964,000 of tenant improvement reimbursements from the landlord. The Company has recorded all tenant improvements as additions to property and equipment and is

amortizing the improvements over the shorter of the estimated useful life of the improvement or the remaining life of the lease. The reimbursements received from the landlord are included in deferred rent liability and amortized over the life of the lease as a contra-expense.

In May 2008, the Company entered into an agreement to sublease 19,558 square feet of its Mountain View facility from May 1, 2008 through April 30, 2009. During the term of the lease, the Company will receive a gross rent of $53,758 per month. There are no options to extend the sublease period, however, if the parties agree to extend the lease term, the monthly sublease rent will be $55,740 per month.

Future minimum lease payments under non-cancelable operating leases, net of sublease income, at December 31, 2008 were as follows (in thousands):

2009	$ 4,558
2010	5,016
2011	5,138
2012	5,263
2013	4,919
Thereafter	20,792
Total minimum payments	$45,686

The above table reflects $215,000 of sublease income in 2009.

Rental expense, net of sublease income, was $4,778,000, $5,402,000, $2,514,000, and $15,921,000, for the years ended December 31, 2008, 2007 and 2006, and for the period from December 19, 2000 (inception) to December 31, 2008, respectively. Rental income from the sublease agreement was $430,000, and $555,000 for the year ended December 31, 2008 and for the period from December 19, 2000 (inception) to December 31, 2008, respectively. The Company received no rental income in the years ended December 31, 2007 and 2006.

Manufacturing and Supply Agreement

On November 2, 2007, The Company entered into a manufacturing and supply agreement, or the supply agreement, with Autoliv ASP, Inc, or Autoliv, relating to the commercial supply of chemical heat packages that can be incorporated into the Company's *Staccato* device. Autoliv had developed these chemical heat packages for us pursuant to a development agreement between Autoliv and the Company executed in October 2005. Under the terms of the supply agreement, Autoliv will develop a manufacturing line capable of producing 10 million chemical heat packages a year. The Company will pay Autoliv $12 million upon the earlier of December 31, 2011 or 60 days after the approval by the Food and Drug Administration of a new drug application filed by the Company. If the agreement is terminated by either party, the Company will be required to reimburse Autoliv up to $12 million for certain expenses related to the equipment and tooling used in the production and testing of the chemical heat packages. Upon payment by the Company, Autoliv will be required to transfer possession and ownership of such equipment and tooling to the Company. Each quarter, with assistance from Autoliv, the Company estimates the amount of work performed on the development of the manufacturing line and recognizes a portion of the total payment related to the manufacturing line as a capital asset and a corresponding non-current liability. As of December 31, 2008, the Company recorded a fixed asset and a non-current liability of $600,000 related to its commitment to Autoliv for the development of the manufacturing line. Autoliv has also agreed to manufacture, assemble and test the chemical heat packages solely for the Company in conformance with the Company's specifications. The Company will pay Autoliv a specified purchase price, which varies based on annual quantities ordered by the Company, per chemical heat package delivered. The initial term of the supply agreement expires on December 31, 2012 and may be extended by written mutual consent.

8. License Agreements

Symphony Allegro, Inc.

On December 1, 2006 (the "Closing Date"), the Company entered into a series of related agreements with Symphony Capital LLC ("Symphony Capital"), Symphony Allegro Holdings LLC ("Holdings") and Holdings' wholly owned subsidiary Symphony Allegro, Inc., ("Allegro") providing for the financing of the clinical development of its AZ-002, *Staccato* alprazolam, and the AZ-004/104, *Staccato* loxapine, product candidates (the "Programs"). The material agreements included the: (i) Purchase Option Agreement by and among Holdings and Allegro and Alexza (the "Purchase Option Agreement"); (ii) Warrant Purchase Agreement between Holdings and Alexza (the "Warrant Purchase Agreement"); (iii) Warrant to Purchase shares of Common Stock issued to Holdings (the "Warrant"); (iv) Amended and Restated Research and Development Agreement by and among Holdings and Allegro and Alexza (the "R&D Agreement"); and (v) Novated and Restated Technology License Agreement by and among Holdings and Allegro and Alexza (the "License Agreement"). Symphony Capital and other investors ("Symphony") invested $50 million in Holdings, which then invested the $50 million in Allegro. Pursuant to the agreements, Allegro agreed to invest up to the full $50 million to fund the clinical development of the Programs, and the Company licensed to Allegro certain intellectual property rights related to these Programs.

Pursuant to the agreements, the Company continues to be primarily responsible for all preclinical, clinical and device development efforts, as well as maintenance of the intellectual property portfolio for the Programs. The Company and Allegro have established a Development Committee to oversee the Programs. The Company participates in the Development Committee and has the right to appoint one of the five members of the board of directors of Allegro.

Pursuant to the agreements, the Company has no further obligation beyond the items described above and the Company has no obligation to the creditors of Allegro as a result of the Company's involvement with Allegro. The investments held by Allegro are to be used to fund the development of the Programs, and are not available for general corporate expenses.

Pursuant to the Warrant Agreement, the Company issued to Holdings a five-year warrant to purchase 2,000,000 shares of the Company's common stock at $9.91 per share. The Warrant, issued upon closing, was assigned a value of $10.7 million using the Black-Scholes valuation model and has been recorded in additional paid in capital.

In consideration for the Warrant, the Company received an exclusive purchase option (the "Purchase Option") that gives the Company the right, but not the obligation, to acquire all, but not less than all, of the equity of Allegro, thereby allowing the Company to reacquire all of the Programs. This Purchase Option is exercisable at any time from December 1, 2007 to December 1, 2010, at predetermined prices that increase over time and range from $67.5 million starting December 31, 2007 to $122.5 million through December 1, 2010. The Purchase Option exercise price may be paid for in cash or in a combination of cash and the Company's common stock, at the Company's sole discretion, provided that the common stock portion may not exceed 40% of the Purchase Option exercise price, or 10% of the Company's common stock issued and outstanding as of the purchase option closing date.

The Company consolidated the financial position and results of operations of Allegro in accordance with FASB Interpretation No. 46, *Consolidation of Variable Interest Entities,* ("FIN 46R"). The Company believes Allegro is by design a variable interest entity as the Company has a purchase option to acquire Allegro's outstanding voting stock at prices that are fixed based upon the date the option is exercised. The fixed nature of the purchase option price limits Symphony's returns, as the investor in Allegro. FIN 46R deems parties to be de facto agents if they cannot sell, transfer, or encumber their interests without the prior approval of an enterprise. Symphony Capital is considered to be a de facto agent of the Company's pursuant to this provision, and because the Company and Symphony, as a related party group, absorb a majority of Allegro's variability, the Company evaluated whether,

pursuant to FIN 46R's requirements, the Company is most closely associated with Allegro. The Company concluded that it is most closely associated with Allegro and should consolidate Allegro because (1) the Company originally developed the technology that was assigned to Allegro, (2) the Company will continue to oversee and monitor the development program, (3) the Company's employees will continue to perform substantially all of the development work, (4) the Company significantly influenced the design of the responsibilities and corporate structure of Allegro, (5) Allegro's operations are substantially similar to the Company's activities, and (6) through the purchase option, the Company has the ability to meaningfully participate in the benefits of a successful development effort.

The noncontrolling interest in Symphony Allegro, Inc., as presented on the consolidated balance sheets, represents Symphony's equity investment in Allegro of $50.0 million equity reduced by $10.7 million for the value of the Purchase Option, and by $2.85 million for a structuring fee and related expenses that the Company paid to Symphony Capital in connection with the closing of the Allegro transaction, resulting in the recording of a net noncontrolling interest of $36.5 million on the effective date. The Company has charged the losses incurred by Allegro to the noncontrolling interest in the determination of the Company's net loss in the consolidated statements of operations and the Company also reduced the noncontrolling interest in the consolidated balance sheets by Allegro's losses. For the years ended December 31, 2008, 2007 and 2006, the net losses of Allegro charged to the noncontrolling interest were $18.6 million, $10.8 million and $1.7 million, respectively. Effective January 1, 2009, the Company will account for the noncontrolling interest in Symphony Allegro in accordance with SFAS 160.

Endo Pharmaceuticals, Inc.

On December 27, 2007, the effective date, the Company entered into a license, development and supply agreement (the "license agreement"), with Endo Pharmaceuticals, Inc. ("Endo") for AZ-003 (*Staccato* fentanyl) and the fentanyl class of molecules for North America. Under the terms of the License Agreement, Endo paid the Company a $10 million upfront fee and Endo was obligated to pay potential additional milestone payments of up to $40 million upon achievement of predetermined regulatory and clinical milestones. Endo was also obligated to pay royalties to the Company on net sales of the product, from which the Company would be required to pay for the cost of goods for the manufacture of the commercial version of the product. Under the terms of the license agreement, the Company had primary responsibility for the development and costs of the *Staccato* Electronic Multiple Dose device and the exclusive right to manufacture the product for clinical development and commercial supply. Endo had the responsibility for future pre-clinical, clinical and regulatory development, and, if AZ-003 was approved for marketing, for commercializing the product in North America. The Company recorded the $10 million upfront fee it received from Endo in January 2008 as deferred revenue. The Company was unable to allocate a fair value to the each of the deliverables outlined in the agreement and therefore accounted for the deliverables as a single unit of accounting. The Company began to recognize the $10 million upfront payment as revenue in the third quarter of 2008 over the estimated performance period of six years, resulting in revenues of $486,000 in 2008.

In January 2009, the Company and Endo mutually agreed to terminate the license agreement, with all rights to AZ-003 reverting back to the Company. The Company's obligations under the license agreement have been fulfilled upon the termination of the agreement, and the Company will recognize the remaining deferred revenue in the first quarter of 2009.

9. Related Party Transactions

Extinguishment of Officer Notes

In December 2005, the Company extinguished the housing loans that were made to three executive officers, the Chief Executive Officer, Senior Vice President of Corporate and Business Development, and Senior Vice President of Research and Development, having an aggregate principal value of $2.3 million and agreed to pay $1.7 million of taxes related to the extinguishment on the officers' behalf. In connection with the loan

extinguishment agreements, the Company entered into a commitment with the officers to settle the loan extinguishment, prior to the closing of the Company's initial public offering, by reducing the aggregate intrinsic value of certain stock option awards to acquire up to 490,908 common shares.

On March 7, 2006 ("the Settlement Date"), in settlement for the extinguishment of the officer housing loans, the Company increased the exercise price on the above mentioned stock option awards held by these officers from $1.10 per share to $8.00 per share, the initial public offering price, which reduced the aggregate intrinsic value of these options by $3.4 million. These options were accounted for as variable awards. As a result of changes in the Company's stock price, the Company recorded a $442,000 reduction in share-based compensation expense during the three months ended March 31, 2006. As the exercise price was fixed in March 2006, the contingency was resolved and variable accounting for these options ceased.

Also on the Settlement Date, the Company entered into amended loan extinguishment agreements with the above mentioned officers, whereby the Company was given the right to increase the exercise price of selected options to $8.00 per share, resulting in an additional reduction in aggregate intrinsic value of $0.6 million. This modification was accounted for under SFAS 123R, and resulted in no additional share-based compensation expense.

Employee Loan

In May 2005, the Company entered into a secured, non-interest bearing promissory note with an employee, the proceeds of which were used to assist with the purchase of a new home. The promissory note was in the amount of $100,000 and was due and payable in May 2010. Since there was no established exchange price or ready market for the employee note, the Company estimated the note's present value using a 5.87% interest rate, resulting in a total note receivable discount and a deferred charge of $25,000. The discount on the note receivable and the deferred charge were being amortized to compensation expense over the five year term. During the years ended December 31, 2007 and 2006, the Company recorded $1,000 and $5,000 of compensation expense and interest income, respectively. In 2007, the note was repaid in full.

10. Common Stock

The Company had reserved shares of common stock for future issuances as of December 31, 2008 as follows:

Stock options outstanding	4,183,348
Unvested restricted stock units outstanding	171,954
2005 Equity Incentive Plan and 2005 Non Employee Director Stock Option Plan — shares available for issuance	1,330,906
Employee Stock Purchase Plan — shares available for issuance	345,495
Warrants outstanding	2,431,242
Total	8,461,845

11. Warrants

In March 2002, in connection with an equipment financing agreement, the Company issued immediately exercisable and fully vested warrants to purchase 21,429 shares of Series B preferred stock at a per share price of $1.40. The warrants expire on the later of April 8, 2013. The Company recorded a deferred financing cost of $27,000 related to the issuance of these warrants. The Company valued these warrants using the Black-Scholes valuation model, assuming an exercise price and fair value of $1.40, an expected volatility of 100%, an expected life of 10 years, an expected dividend yield of 0%, and a risk-free interest rate of 4.61%. The estimated fair value of the warrants is recorded as debt discount. This amount is amortized to interest expense over the commitment term of the

equipment financing agreement. In 2006, the warrant was converted to purchase 4,116 shares of common stock at a price of $7.29 per share. As of December 31, 2008, this warrant remained outstanding and exercisable.

In January and September 2003, in connection with the modifications of an equipment financing agreement, the Company issued immediately exercisable and fully vested warrants to purchase 24,058 and 19,247 shares of Series C preferred stock, respectively, at a per share price of $1.56. The warrants expire April 8, 2013. The Company valued these warrants using the Black-Scholes valuation model, assuming an exercise price and fair value of $1.56, an expected volatility of 100%, an expected life of 10 years, an expected dividend yield of 0%, and risk-free interest rate of 4.05% and 4.45%, respectively. The estimated fair values of $35,000 and $27,000, respectively, are recorded as debt discount and are being amortized to interest expense over the remaining commitment term of the financing agreement. In 2006, these warrants were converted into warrants to purchase 4,852 shares and 3,882 shares of common stock, both at a price of $7.74 shares. As of December 31, 2008, both of these warrants remained outstanding and exercisable.

In March 2004, in connection with the modifications of an equipment financing agreement, the Company issued immediately exercisable and fully vested warrants to purchase 14,232 shares of Series C preferred stock at a per share price of $1.56. The warrants expire on April 8, 2013. The Company valued these warrants using the Black-Scholes valuation model, assuming an exercise price and fair value of $1.56, an expected volatility of 100%, an expected life of 10 years, an expected dividend yield of 0%, and risk-free interest rate of 4.35%. The estimated fair value of $20,000 was recorded as debt discount and amortized to interest expense over the remaining commitment term of the financing agreement. In 2006, the warrant was converted into a warrant to purchase 2,870 shares of common stock at a price of $7.74. As of December 31, 2008, these warrants remained outstanding and exercisable.

In December 2006, in connection with the Symphony Allegro transaction (see Note 8), the Company issued to Holdings a five-year warrant to purchase 2,000,000 shares of the Company's common stock at $9.91 per share. The warrants issued upon closing were assigned a value of $10.7 million in accordance with the Black-Scholes option valuation methodology assuming an exercise price of $9.91, an expected volatility of 80%, an expected life of 5 years, an expected dividend yield of 0% and risk-free interest rate of 4.45%. This fair value has been recorded as a reduction to the noncontrolling interest in Symphony Allegro. This warrant remains outstanding at December 31, 2008.

In March 2008, in connection with the registered direct equity issuance to Bio*One described in Note 1, the Company issued a warrant to Bio*One to purchase up to 375,000 of additional shares of Alexza common stock at a purchase price per share of $8.00. As outlined in the agreement, the warrant was subject to the same price adjustment as the common stock sale, and effective January 1, 2009 the warrant was adjusted to purchase 415,522 shares at a purchase price of $7.22 per share. The Company committed to initiate and maintain manufacturing operations in Singapore, and the warrant was to become exercisable only if the Company terminates operations in Singapore or does not achieve certain performance milestones. The warrant has a maximum term of 5 years. Net proceeds from the sale of the stock and warrant were approximately $9.84 million after deducting offering expenses. The warrant has been recorded as equity in accordance with the provisions of EITF Issue No. 00-19, *Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company's Own Stock*. The settlement of the warrant is within the Company's control. Specifically, the Company shall use commercially reasonable efforts to maintain an effective registration statement. However, if the registration statement is not effective at the time the warrant is exercised, then the holder is only able to exercise the warrant by means of a cashless exercise. In December 2008, the Company did not meet its defined performance milestone, and as a result the warrant became fully exercisable. This warrant remains outstanding at December 31, 2008.

12. Equity Incentive Plans

2005 Equity Incentive Plan

In December 2005, the Company's Board of Directors adopted the 2005 Equity Incentive Plan (the "2005 Plan") and authorized for issuance thereunder 1,088,785 shares of common stock. The 2005 Plan became effective upon the closing of the Company's initial public offering on March 8, 2006. The 2005 Plan is an amendment and restatement of the Company's previous stock option plans. Stock options issued under the 2005 Plan generally vest over 4 years, vesting is generally based on service time, and have a maximum contractual term of 10 years.

In the third quarter of 2006, the Company began issuing restricted stock units to non-officer employees. Beginning in 2009, the Company began issuing restricted stock units to both officers and to non-employee directors. Restricted stock unit issuances to non-employee directors were made in lieu of paying cash director fees. Restricted stock units granted to officer or non-officer employees generally vest over a four-year period from the grant date. Restricted stock units granted to non-employee directors generally vest one year after the date of grant. Prior to vesting, restricted stock units do not have dividend equivalent rights, do not have voting rights and the shares underlying the restricted units are not considered issued and outstanding. Shares are issued on the date the restricted stock units vest.

The 2005 Plan provides for annual reserve increases on the first day of each fiscal year commencing on January 1, 2007 and ending on January 1, 2015. The annual reserve increases will be equal to the lesser of (i) 2% of the total number of shares of the Company's common stock outstanding on December 31 of the preceding calendar year, or (ii) 1,000,000 shares of common stock. The Company's Board of Directors has the authority to designate a smaller number of shares by which the authorized number of shares of common stock will be increased prior to the last day of any calendar year. In May 2008, the Company's stockholders approved an amendment to the plan to increase the number of shares of the Company's stock reserved for issuance under the 2005 Plan by an additional 1,500,000 shares.

2005 Non-Employee Directors' Stock Option Plan

In December 2005, the Company's Board of Directors adopted the 2005 Non-Employee Directors' Stock Option Plan (the "Directors' Plan") and authorized for issuance thereunder 250,000 shares of common stock. The Directors' Plan became effective immediately upon the closing of the Company's initial public offering on March 8, 2006. The Directors' Plan provides for the automatic grant of nonstatutory stock options to purchase shares of common stock to the Company's non-employee directors, which vest over four years and have a term of 10 years. The Directors' Plan provides for an annual reserve increase to be added on the first day of each fiscal year, commencing on January 1, 2007 and ending on January 1, 2015. The annual reserve increases will be equal to the number of shares subject to options granted during the preceding fiscal year less the number of shares that revert back to the share reserve during the preceding fiscal year. The Company's Board of Directors has the authority to designate a smaller number of shares by which the authorized number of shares of common stock will be increased prior to the last day of any calendar year.

The following table sets forth the summary of stock option activity under the Equity Incentive Plans:

	Outstanding Options	
	Number of Shares	Weighted Average Exercise Price
Options granted	298,351	$0.34
Options exercised	(9,090)	$0.22
Balance as of December 31, 2001	289,261	$0.34
Options granted	210,777	$1.03
Options exercised	(65,942)	$0.84
Options forfeited	(10,909)	$0.22
Balance as of December 31, 2002	423,187	$0.61
Options granted	703,486	$1.10
Options exercised	(74,904)	$0.60
Options forfeited	(50,092)	$0.57
Balance as of December 31, 2003	1,001,677	$0.95
Options granted	893,952	$1.10
Options exercised	(100,192)	$0.74
Options forfeited	(132,641)	$1.08
Balance as of December 31, 2004	1,662,796	$1.04
Options granted	824,035	$2.86
Options exercised	(380,501)	$0.94
Options forfeited	(98,310)	$1.08
Balance as of December 31, 2005	2,008,020	$1.80
Options granted	848,075	$7.71
Options exercised	(160,662)	$1.28
Options forfeited	(82,938)	$2.00
Options cancelled	(1,453)	$8.64
Balance as of December 31, 2006	2,611,042	$5.23
Options granted	1,054,656	$9.10
Options exercised	(204,423)	$2.11
Options forfeited	(249,536)	$6.98
Options cancelled	(4,875)	$6.60
Balance as of December 31, 2007	3,206,864	$6.56
Options granted	1,472,171	$5.26
Options exercised	(104,428)	$1.55
Options forfeited	(190,284)	$7.20
Options cancelled	(200,975)	$7.81
Balance as of December 31, 2008	4,183,348	$6.14
Options exercisable at:		
December 31, 2006	901,425	$4.74
December 31, 2007	1,365,538	$5.54
December 31, 2008	1,950,662	$6.02

The total intrinsic value of options exercised during the years ended December 31, 2008, 2007, and 2006 was $463,000, $1,662,000, and $1,003,000, respectively. None of the Company's options have expired.

Information regarding the stock options outstanding at December 31, 2008 is summarized below:

	Outstanding			Exercisable		
Exercise Price	Number of Shares	Remaining Contractual Life (In Years)	Aggregate Intrinsic Value	Number of Shares	Remaining Contractual Life (In Years)	Aggregate Intrinsic Value
$1.10 - 1.38	606,087	5.89	$1,197,000	539,132	5.87	$1,068,000
2.64 - 4.24	243,680	8.58	4,000	58,624	7.03	—
4.35 - 4.35	523,700	9.52	—	—	—	—
4.41 - 6.24	482,900	9.35	—	5,466	9.40	—
6.55 - 7.20	597,323	7.85	—	348,338	7.76	—
7.30 - 7.90	155,722	8.75	—	58,854	8.67	—
8.00 - 8.00	600,457	5.63	—	530,430	5.45	—
8.01 - 8.89	625,420	8.46	—	236,620	8.41	—
8.91 - 11.70	348,059	8.15	—	173,198	8.09	—
	4,183,348	7.82	$1,201,000	1,950,662	6.73	$1,068,000

The intrinsic value is calculated as the difference between the market value as of December 31, 2008 and the exercise price of the shares. The market value as of December 31, 2008 was $3.17 as reported by the NASDAQ Stock Market.

Information with respect to nonvested share units (restricted stock units) as of December 31, 2008 is as follows:

	Number of Shares	Weighted Average Grant - Date Fair Value
Outstanding at January 1, 2006	—	$ —
Granted	34,680	7.00
Released	—	—
Forfeited	(600)	7.00
Outstanding at December 31, 2006	34,080	7.00
Granted	74,575	8.89
Released	(8,245)	7.00
Forfeited	(7,285)	7.71
Outstanding at December 31, 2007	93,125	8.42
Granted	112,423	4.35
Released	(23,443)	8.33
Forfeited	(10,151)	7.00
Outstanding at December 31, 2008	171,954	5.86

The total intrinsic value of restricted stock units released during the years ended December 31, 2008 and 2007 was $131,000 and $68,000, respectively, the Company did not have any restricted stock units released during the year ended December 31, 2006.

The Company authorized shares of common stock for issuance under the Plans as follows.

Year	Number of Shares
2001	363,636
2002	770,732
2003	454,545
2004	1,000,000
2005	25,544
2006	1,327,990
2007	676,386
2008	2,174,840

As of December 31, 2008, 1,330,906 shares remained available for issuance under the 2005 Plan and the Directors' Plan.

On January 1, 2009 an additional 693,917 shares were authorized for issuance under the evergreen provisions of the 2005 Plan and the Directors' Plan.

2005 Employee Stock Purchase Plan

In December 2005, the Company's Board of Directors adopted the 2005 Employee Stock Purchase Plan ("ESPP") and authorized for issuance thereunder 500,000 shares of common stock. The ESPP allows eligible employee participants to purchase shares of the Company's common stock at a discount through payroll deductions. The ESPP consists of a fixed offering period, generally twenty-four months with four purchase periods within each offering period. Purchases are generally made on the last trading day of each October and April. Employees purchase shares at each purchase date at 85% of the market value of our common stock on their enrollment date or the end of the purchase period, whichever price is lower. The Company issued 305,146, 205,870, and 131, 682 shares at a weighted average prices of $3.84, $6.83, and $6.80 in 2008, 2007, and 2006, respectively.

The ESPP provides for annual reserve increases on the first day of each fiscal year commencing on January 1, 2007 and ending on January 1, 2015. The annual reserve increases will be equal to the lesser of (i) 1% of the total number of shares of the Company's common stock outstanding on December 31 of the preceding calendar year, or (ii) 250,000 shares of common stock. The Company's Board of Directors has the authority to designate a smaller number of shares by which the authorized number of shares of common stock will be increased prior to the last day of any calendar year. On January 1, 2008 and 2007 an additional 250,000 and 238,193 shares, respectively, were reserved for issuance under this provision. At December 31, 2008, 345,495 shares are available for issuance under the ESPP.

On January 1, 2009 an additional 250,000 shares were reserved for issuance under the ESPP.

13. 401(k) Plan

The Company sponsors a 401(k) Plan that stipulates that eligible employees can elect to contribute to the 401(k) Plan, subject to certain limitations. Pursuant to the 401(k) Plan, the Company does not match any employee contributions.

14. Government Research Grants

The Company has been awarded grants from the National Institute of Health ("NIH") for various research and development projects. The Company's federal government research grants provide for the reimbursement of

qualified expenses for research and development as defined under the terms of each grant. As of December 31, 2008 and 2007, the Company had no NIH grants in place.

15. Income Taxes

There is no provision for income taxes because the Company has incurred operating losses since inception.

The reported amount of income tax expense attributable to operations for the year differs from the amount that would result from applying domestic federal statutory tax rates to loss before income taxes from operations as summarized below (in thousands):

	Year Ended December 31,		
	2008	2007	2006
		(In thousands)	
Federal tax benefit at statutory rate	$(19,873)	$(15,321)	$(14,214)
State tax benefit net of federal effect	(3,402)	(2,629)	(2,436)
Research and development credits	(2,693)	(3,538)	(1,189)
Other permanent differences	19	20	17
Share-based compensation	1,450	274	543
Change in valuation allowance	24,567	21,193	17,317
Other	(68)	1	(38)
Total	$ —	$ —	$ —

Deferred income taxes reflect the net tax effects of the temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amount used for income tax purposes. The deferred tax asset was calculated using an effective tax rate of 40%. Significant components of the Company's deferred tax assets are as follows:

	December 31,	
	2008	2007
	(In thousands)	
Federal and state net operating loss carryforwards	$ 58,451	$ 60,516
Federal and state research and development credit carryforwards	10,210	7,093
Accrued liabilities	2,736	287
Capitalized research and development costs	23,216	829
Other	42	678
Total deferred tax assets	94,655	69,403
Valuation allowance	(94,655)	(69,403)
Net deferred tax assets	$ —	$ —

The Company's accounting for deferred taxes under SFAS No. 109, *Accounting for Income Taxes*, involves the evaluation of a number of factors concerning the realizability of the Company's net deferred tax assets. The Company primarily considered such factors as the Company's history of operating losses, the nature of the Company's deferred tax assets and the timing, likelihood and amount, if any, of future taxable income during the periods in which those temporary differences and carryforwards become deductible. At present, the Company does not believe that it is more likely than not that the deferred tax assets will be realized; accordingly, a full valuation allowance has been established and no deferred tax asset is shown in the accompanying balance sheets. The

valuation allowance increased by approximately $25,252,000 and $20,847,000 during the years ended December 31, 2008 and 2007, respectively.

As of December 31, 2008 the Company had federal net operating loss carryforwards of approximately $149,137,000. The Company also had federal research and development tax credit carryforwards of approximately $6,862,000. The net operating loss and tax credit carryforwards will expire at various dates beginning in 2020, if not utilized.

As of December 31, 2008, the Company had state net operating loss carryforwards of approximately $140,525,000, which will begin to expire in 2012. The Company also had state research and development tax credit carryforwards of approximately $4,954,000, which have no expiration, and a Manufacturer's Investment Credit of $78,000, which will begin to expire in 2009, if not utilized.

As of December 31, 2008, approximately $455,000 of deferred tax assets is attributable to certain employee stock option deductions and the federal and state net operating loss carryforward has been adjusted accordingly. When realized, the benefit of the tax deduction related to these options will be accounted for as a credit to stockholders' equity rather than as a reduction of the income tax provision.

Utilization of the net operating loss carryforwards and credits may be subject to an annual limitation with substantial effect, due to the ownership change limitations provided by the Internal Revenue Code that are applicable if the Company experiences an "ownership change". That may occur, for example, as a result of the initial public offering aggregated with certain other sales of our stock.

The Company recognized an, increase to the deferred tax assets in 2007,to decrease its reserve for unrecognized tax benefits as a result of the implementation of FIN 48. Because of the correlative reduction in the Company's full valuation allowance, this adjustment did not result in a credit to deficit accumulated during development stage. During 2008, the Company performed an analysis of its research and development credits. As a result of this analysis, the Company decreased its reserve for unrecognized tax benefits related to research and development credits from 25% for both federal and state taxes to 10% for federal taxes and 20% for state taxes. Because of the correlative reduction in the Company's full valuation allowance, this adjustment did not result in a credit to the statement of operations.

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows:

Balance at January 1, 2007	$ 1,635
Additions based on tax positions taken during a prior period	—
Reductions based on tax positions taken during a prior period	—
Additions based on tax positions taken during the current period	611
Reductions based on tax positions taken during the current period	—
Reductions related to settlement of tax matters	—
Reductions related to a lapse of applicable statute of limitations	—
Balance at December 31, 2007	$ 2,246
Additions based on tax positions taken during a prior period	—
Reductions based on tax positions taken during a prior period	(1,067)
Additions based on tax positions taken during the current period	401
Reductions based on tax positions taken during the current period	—
Reductions related to settlement of tax matters	—
Reductions related to a lapse of applicable statute of limitations	—
Balance at December 31, 2008	$ 1,580

The Company has not incurred any interest or penalties as of December 31, 2008. The Company does not anticipate any significant change within 12 months of this reporting date of its uncertain tax positions. The Company is subject to taxation in the US and various states jurisdictions. There are no ongoing examinations by taxing authorities at this time. The Company's various tax years starting with 2000 to 2007 remain open in various taxing jurisdictions.

16. Development Agreement

In October 2005, the Company entered into a development agreement with Autoliv ASP, Inc. ("Autoliv") for the development of heat packages that can be incorporated into the Company's proprietary single dose drug delivery device for sale by the Company. Under the terms of the development agreement, Autoliv and the Company agreed to contribute $2,500,000 each toward the development efforts. The Company's contribution was expected to include approximately $1,750,000 for purchases of equipment and $750,000 for co-development efforts. Equipment purchased by the Company is owned by the Company. In 2008, 2007 and 2006 the Company paid $83,000, $334,000 and $333,000, respectively, to Autoliv for co-development fees under the agreement.

On November 2, 2007, the Company entered into a Manufacturing and Supply Agreement, ("Supply Agreement"), with Autoliv relating to the commercial supply of heat packages that can be incorporated into its *Staccato* device (the "Chemical Heat Packages"). Under the terms of the Supply Agreement, Autoliv will develop a manufacturing line capable of producing 10 million Chemical Heat packages a year. The Company will pay Autoliv $12 million upon the earlier of December 31, 2011, or 60 days after the approval by the FDA of an NDA filed by the Company. If either party terminates the Supply Agreement the Company will be required to reimburse Autoliv for certain expenses related to the equipment and tooling used in the production and testing of the Chemical Heat Packages up to $12 million. Upon either payment, Autoliv will be required to transfer possession and ownership of such equipment and tooling to the Company. The Company estimates the amount of work performed on the development of the manufacturing line and recognizes a portion of the total payment related to the manufacturing line as a capital asset and a corresponding non-current liability. As of December 31, 2008, the Company has recorded a fixed asset and a non-current liability of $600,000 related to its commitment to Autoliv for the development of the manufacturing line.

Autoliv has agreed to manufacture, assemble and test the Chemical Heat Packages solely for the Company in conformance with the Company's specifications. The Company will pay Autoliv a specified purchase price, which varies based on annual quantities ordered by the Company, per Chemical Heat Package delivered. The initial term of the Supply Agreement expires on December 31, 2012 and may be extended by mutual written consent. The Supply Agreement provides that during the term of the Supply Agreement, Autoliv will be the Company's exclusive supplier of the Chemical Heat Packages. In addition, the Supply Agreement grants Autoliv the right to negotiate for the right to supply commercially any second generation chemical heat package (a "Second Generation Product") and provides that the Company will pay Autoliv certain royalty payments if the Company manufactures Second Generation Products itself or if the Company obtains Second Generation Products from a third party manufacturer. Upon the expiration or termination of the Supply Agreement the Company will be required, on an ongoing basis, to pay Autoliv certain royalty payments related to the manufacture of the Chemical Heat Packages by the Company or third party manufacturers. No Chemical Heat Packages have been purchased under this agreement as of December 31, 2008.

17. Subsequent Events

In January 2009, the Company consolidated its operations, with a primary focus on the continued rapid development of AZ-004. The restructuring included a workforce reduction of 52 employees, representing approximately 33% of the Company's total workforce In addition, the Company announced that it would not commit additional resources to the development of AZ-003 in 2009 as a result of the termination of the Endo license, development and supply agreement (See Note 8).

18. Quarterly Results (Unaudited)

The following table is in thousands, except per share amounts:

	Quarter Ended			
	March 31	June 30	September 30	December 31
Fiscal 2008				
Loss from operations	$(19,155)	$(20,500)	$(21,067)	$(17,998)
Loss before noncontrolling interest in Symphony Allegro, Inc.	(18,366)	(20,013)	(20,758)	(17,904)
Net loss	(14,609)	(14,122)	(14,692)	(15,027)
Basic and diluted net loss per share	(0.47)	(0.43)	(0.45)	(0.46)
Shares used in computation of basic and diluted net loss per share	31,225	32,532	32,610	32,821
Fiscal 2007				
Loss from operations	$(13,820)	$(14,159)	$(15,136)	$(17,418)
Loss before noncontrolling interest in Symphony Allegro, Inc.	(12,998)	(12,922)	(13,717)	(16,273)
Net loss	(10,916)	(10,278)	(10,752)	(13,173)
Basic and diluted net loss per share	(0.46)	(0.36)	(0.35)	(0.42)
Shares used in computation of basic and diluted net loss per share	23,869	28,480	30,975	31,097

Item 9. ***Changes in and Disagreements With Accountants on Accounting and Financial Disclosure***

Not Applicable.

Item 9A. ***Controls and Procedures***

Evaluation of Disclosure Controls and Procedures:

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our Exchange Act reports is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow for timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and in reaching a reasonable level of assurance, management is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

As of December 31, 2008, the end of the period covered by this report, we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures. Based on the foregoing, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting:

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rules 13a-15(f) and 15d-15(f). Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2008 based on the framework in *Internal Control — Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on that evaluation, our management concluded that our internal control over financial reporting was effective as of December 31, 2008. Our independent registered public accounting firm, Ernst &Young LLP, audited the consolidated financial statements included in this Annual Report on Form 10-K and have issued an audit report on the effectiveness of our internal control over financial reporting. Their report on the audit of internal control over financial reporting appears below.

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders
Alexza Pharmaceuticals, Inc.

We have audited Alexza Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2008, based on criteria established in Internal Control — Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). Alexza Pharmaceuticals, Inc.'s management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Annual Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, Alexza Pharmaceuticals, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2008, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Alexza Pharmaceuticals, Inc. (a development stage company) as of December 31, 2008 and 2007, and the related consolidated statements of operations, convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2008 and for the period from December 19, 2000 (inception) to December 31, 2008 of Alexza Pharmaceuticals, Inc. and our report dated March 9, 2009, expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Palo Alto, California
March 9, 2009

Changes in Internal Control Over Financial Reporting:

There has been no change in our internal control over financial reporting during our most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. ***Other Information***

None.

PART III

Item 10. ***Directors and Executive Officers of the Registrant***

The information required by this Item concerning our directors is incorporated by reference to the information to be set forth in the sections entitled "Proposal No. 1 — Election of Directors" and "Section 16(a) Beneficial Ownership Reporting Compliance" in our definitive Proxy Statement for the 2009 Annual Meeting of Stockholders to be filed within 120 days after the end of the Registrant's fiscal year ended December 31, 2008, or the Proxy Statement. The information required by this Item concerning our executive officers is incorporated by reference to the information to be set forth in the section of the Proxy Statement entitled "Executive Officers." Information regarding compliance with Section 16(a) of the Exchange Act, our code of business conduct and ethics and certain information related to our Audit Committee and Ethics Committee is set forth under the heading "Information Regarding the Board of Directors and Corporate Governance" in our Proxy Statement, and is incorporated herein by reference thereto.

Item 11. ***Executive Compensation***

The information required by this Item 11 is incorporated by reference to the information under the caption "Executive Compensation" in the Proxy Statement to be filed with the Securities and Exchange Commission no later than 120 days from the end of our last fiscal year.

Item 12. ***Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters***

The information required by this Item 12 with respect to stock ownership of certain beneficial owners and management and securities authorized for issuance under equity compensation plans are incorporated by reference to the information under the caption "Security Ownership of Certain Beneficial Owners and Management" in the Proxy Statement.

Securities Authorized For Issuance Under Equity Compensation Plans

We maintain the 2005 Equity Incentive Plan, 2005 Non-Employee Directors' Stock Option Plan and 2005 Employee Stock Purchase Plan pursuant to which we may grant equity awards to eligible persons.

The following table gives information about equity awards under our 2005 Equity Incentive Plan, 2005 Non-Employee Directors' Stock Option Plan and 2005 Employee Stock Purchase Plan as of December 31, 2008.

Plan Category	(a) Number of Securities to be Issued upon Exercise of Outstanding Options, Warrants and Rights	(b) Weighted-Average Exercise Price of Outstanding Options, Warrants and Rights	(c) Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (Excluding Securities Reflected in Column (a))
Equity compensation plans approved by security holders	4,355,302	$5.90	1,676,401(1)(2)
Equity compensation plans not approved by security holders	—	—	—
Total	4,355,302	$5.90	1,676,401

(1) The 2005 Plan incorporates an evergreen formula pursuant to which on each January 1, the aggregate number of shares reserved for issuance under the 2005 Plan will increase by a number equal to the lesser of (i) 1,000,000 shares, (ii) 2% of the outstanding shares on December 31 of the preceding calendar year, or (iii) an amount determined by our Board.

The Directors' Plan incorporates an evergreen formula pursuant to which on each January 1, the aggregate number of shares reserved for issuance under the Director's Plan will increase by the number of shares subject to options granted during the preceding calendar year less the number of shares that revert back to the share reserve during the preceding calendar year.

The ESPP incorporates an evergreen formula pursuant to which on each January 1, the aggregate number of shares reserved for issuance under the ESPP will increase by a number equal to the lesser of (i) 250,000 shares, (ii) 1% of the outstanding shares on December 31 of the preceding calendar year, or (iii) an amount determined by our Board.

(2) Of these shares, 345,495 shares remain available for purchase under the ESPP.

Item 13. ***Certain Relationships and Related Transactions and Director Independence***

The information required in this Item 13 is incorporated by reference to the information under the caption "Certain Relationships and Related Transactions and Director Independence" in the Proxy Statement.

Item 14. ***Principal Accountant Fees and Services***

The information required by this Item 14 under the caption "Principal Accountant Fees and Services" is incorporated by reference to the information in the Proxy Statement.

PART IV

Item 15. ***Exhibits and Financial Statement Schedules***

(a) 1. *Financial Statements*

See Index to Financial Statements under Item 8 on page 66

(a) 2. *Financial Statement Schedules*

All schedules are omitted because they are not applicable or are not required or the information required to be set forth therein is included in the Financial Statements or notes thereto.

(a) 3. *Exhibits*

EXHIBIT INDEX

Exhibit Number	Description of Document
3.5	Restated Certificate of Incorporation(1)
3.7	Amended and Restated Bylaws(1)
3.8	Amendment to Amended and Restated Bylaws(5)
4.1	Specimen Common Stock Certificate(1)
4.2	Second Amended and Restated Investors' Rights Agreement between Registrant and certain holders of Preferred Stock dated November 5, 2004(1)
10.2	Form of Director/Officer Indemnification Agreement entered into between Registrant and each of its directors and officers(9)*
10.3◆	Form of Change of Control Agreement*
10.4	2005 Equity Incentive Plan(8)*
10.5	Form of Option Grant Notice, Form of Option Agreement and Form of Notice of Exercise to 2005 Equity Incentive Plan(1)*
10.6	2005 Non-Employee Directors' Stock Option Plan(1)
10.7	Form of Option Grant Notice, Form of Option Agreement and Form of Notice of Exercise to 2005 Non-Employee Directors' Stock Option Plan(1)
10.8	2005 Employee Stock Purchase Plan(1)*
10.9	Form of Offering Document to 2005 Employee Stock Purchase Plan(1)*
10.10	Lease between Registrant and California Pacific Commercial Corporation dated March 20, 2002(1)
10.11	First Amendment to Lease between Registrant and California Pacific Commercial Corporation dated May 8, 2003(1)
10.12	Second Amendment to Lease between Registrant and California Pacific Commercial Corporation dated February 11, 2005(1)
10.13	Development Agreement between Registrant and Autoliv ASP, Inc. dated October 3, 2005(1)
10.14	Loan and Security Agreement between Registrant and Silicon Valley Bank dated March 20, 2002, as amended on January 7, 2003, September 3, 2003, March 18, 2004 and May 16, 2005(1)
10.15	Master Security Agreement between Registrant and General Electric Capital Corporation dated May 17, 2005, as amended on May 18, 2005(1)
10.16	Promissory Note between Registrant and General Electric Capital Corporation dated June 15, 2005(1)
10.17	Promissory Note between Registrant and General Electric Capital Corporation dated August 24, 2005(1)
10.20	Warrant to Purchase shares of Series B Preferred Stock issued to Silicon Valley Bank dated March 20, 2002(1)
10.21	Warrant to Purchase shares of Series C Preferred Stock issued to Silicon Valley Bank dated January 7, 2003, as amended on March 4, 2003(1)
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10.23	Warrant to Purchase shares of Series C Preferred Stock issued to Silicon Valley Bank dated April 7, 2004(1)
10.24	Lease Agreement between the Brittania, LLC and the Registrant dated August 25, 2006(2)
10.26†	Purchase Option Agreement by and among Symphony Allegro Holdings LLC and Symphony Allegro, Inc. and Registrant dated December 1, 2006(2)
10.27	Warrant Purchase Agreement between Symphony Allegro Holdings LLC and Registrant dated December 1, 2006(2)
10.28	Warrant to Purchase shares of Common Stock issued to Symphony Allegro Holdings LLC dated December 1, 2006(2)
10.29†	Amended and Restated Research and Development Agreement by and among Symphony Allegro Holdings LLC and Symphony Allegro, Inc. and Registrant dated December 1, 2006(2)

Exhibit Number	Description of Document
10.30	Registration Rights Agreement between Symphony Allegro Holdings LLC and Registrant dated December 1, 2006(2)
10.31†	Novated and Restated Technology License Agreement by and among Symphony Allegro Holdings LLC and Symphony Allegro, Inc. and Registrant dated December 1, 2006(2)
10.32	Confidentiality Agreement by and among Symphony Allegro Holdings LLC and Symphony Allegro, Inc. and Registrant dated December 1, 2006(2)
10.33	2007 Performance Bonus Program*(2)
10.34	First Amendment to Lease between Britannia Hacienda VIII LLC and the Registrant dated May 4, 2007(3)
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10.36†	Manufacturing and Supply Agreement between Registrant and Autoliv ASP, Inc., dated November 2, 2007(5)
10.38	Offer Letter between the Registrant and Michael Simms, dated January 23, 2008(5)
10.39	Stock and Warrant Purchase Agreement between Registrant and Biomedical Investment Fund Pte Ltd., dated March 26, 2008(6)
10.40	Warrant to Purchase shares of Common Stock issued to Biomedical Investment Fund Pte Ltd. dated March 27, 2008(6)
10.41	Common Stock Purchase Agreement between Registrant and Azimuth Opportunity Ltd. dated March 31, 2008(7)
10.42◆	Form of Notice of Grant of Award and Stock Unit Award Agreement to 2005 Equity Incentive Plan
10.43	2006 Performance Bonus Program*(10)
10.44	2008 Performance Bonus Program*(11)
10.45	2009-2010 Performance Based Incentive Program*(12)
14.1	Alexza Pharmaceuticals, Inc. Code of Business Conduct for Employees, Executive Officers and Directors(2)
21.1◆	Subsidiaries of Registrant
23.1◆	Consent of Independent Registered Public Accounting Firm
24.1◆	Power of Attorney included on the signature pages hereto
31.1◆	Section 302 Certification of CEO.
31.2◆	Section 302 Certification of CFO.
32.1◆	Section 906 Certifications of CEO and CFO.

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* Management contract or compensation plan or arrangement.

◆ Filed herein

† Confidential treatment has been granted with respect to certain portions of this exhibit. This exhibit omits the information subject to this confidentiality request. Omitted portions have been filed separately with the SEC.

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(1) Incorporated by reference to exhibits to our Registration Statement on Form S-1 filed on December 22, 2005, as amended (File No. 333-130644)

(2) Incorporated by reference to our Annual Report on Form 10-K (File No. 000-51820) as filed with the SEC on March 29, 2007.

(3) Incorporated by reference to our Quarterly Report on Form 10-Q (File No. 000-51820) as filed with the SEC on August 13, 2007

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(12) Incorporated by reference to our Current Report on Form 8-K (File No. 000-51820) as filed with the SEC on February 24, 2009.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

ALEXZA PHARMACEUTICALS, INC.

By: /s/ THOMAS B. KING
Thomas B. King
President and Chief Executive Officer

Dated: March 10, 2009

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Thomas B. King and August J. Moretti, and each of them, as his true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him and in his name, place, and stead, in any and all capacities, to sign any and all amendments to this Report, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming that all said attorneys-in-fact and agents, or any of them or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Exchange Act, this report has been signed below by the following persons on behalf of the Registrant and in the capacities indicated on March 10, 2009.

Signature	Title
/s/ THOMAS B. KING Thomas B. King	President, Chief Executive Officer and Director (Principal Executive Officer)
/s/ AUGUST J. MORETTI August J. Moretti	Senior Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)
/s/ HAL V. BARRON Hal V. Barron	Director
/s/ SAMUEL D. COLELLA Samuel D. Colella	Director
/s/ ALAN D. FRAZIER Alan D. Frazier	Director
/s/ DEEPIKA R. PAKIANATHAN Deepika R. Pakianathan	Director

Signature	Title
/s/ J. LEIGHTON READ J. Leighton Read	Director
/s/ GORDON RINGOLD Gordon Ringold	Director
/s/ ISAAC STEIN Isaac Stein	Director

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(12) Incorporated by reference to our Current Report on Form 8-K (File No. 000-51820) as filed with the SEC on February 24, 2009.

Safe Harbor Statement This annual report includes forward-looking statements that involve significant risks and uncertainties. Any statement describing the Company's expectations or beliefs is a forward-looking statement 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. Risks concerning the Company's business are described in additional detail under the heading "Risk Factors" of the Company's Annual Report on Form 10-K for the year ended December 31, 2008 and the Company's periodic and current reports. Forward-looking statements contained in this annual report 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.

Design Hane Chow, Inc., Oakland, CA | **Photography** Anne Knudsen, Palo Alto, CA | **Illustrations** Paul Wearing, London, UK

Alexza Pharmaceuticals is a pharmaceutical development company focused on the research, development, and commercialization of novel proprietary products for the treatment of acute and intermittent medical conditions of the central nervous system. The company's proprietary *Staccato* system — which delivers pure aerosolized drug to deep lung tissues through one simple breath — is intended to provide uniquely fast and patient-friendly therapeutic effect. Alexza currently has six products in development targeting CNS conditions such as acute agitation, migraine headaches, breakthrough pain, and sleeplessness.

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