



ALEXZA PHARMACEUTICALS  
2009 annual report

understanding agitation...

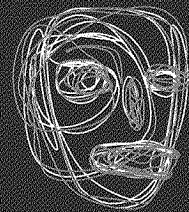
...it's like anger and streng

I'm out of control

feeling disconnected

angry

...means understanding the patient need



verbally abusive

violent

distressed

overwhelm  
grouch  
restless

nervous

nauseous racing heart rate racing blood

I completely lost control  
feels like you're not even there like you're standing  
and observing you would like to stop yourself  
but it's going on really

na



dysfunctional

violent  
blacking out

out of control

psychotic  
shaking

poor impulse control

cursing

HOSTILITY

panic

For **8.1** million US patients with bipolar disorder and schizophrenia, acute agitation is a debilitating and dangerous condition

cold sweats

sleeplessness

anguish

no concentration

**AGITATION IS A CONDITION THAT AFFECTS** many people with major central nervous system disorders, from neurodegenerative diseases like Parkinson's and Alzheimer's to a variety of psychiatric diseases. In the United States alone, there are approximately 2.4 million adults with schizophrenia and 5.7 million adults with bipolar disorder, approximately 90% of whom suffer agitation. These same patients average 11 to 12 agitation episodes per year.


Agitation is characterized by a steadily growing sense of unease, tension and restlessness. Episodes generally escalate over time — several hours to several days — and as the agitation intensifies, individual behavior grows more excitable, uncontrolled, and potentially violent. Patients with schizophrenia or bipolar disorder can recognize that an episode is escalating, but current early-intervention treatment options are limited.

Most patients experiencing agitation are not treated until the episode has grown into a crisis. Alexza's market research shows that approximately 50% of treated agitation episodes are addressed in hospital emergency

settings. Another 35% are handled in inpatient psychiatric hospitals or long-term care facilities. An additional 15% are treated in a physician's office or similar environment.

Because patients whose agitation has reached the point of emergency medical intervention are often frightened, anguished, and dysfunctional, the typical treatment is an intramuscular injection (often with the patient in restraints) to ensure fast and reliable effect. For the patient, the experience is invasive, disorienting and humiliating. For the medical professional, it can be dangerous and is often unrewarding since such treatment prevents establishing the patient trust needed to create a therapeutic alliance for successful longer-term treatment.

Alexza believes that agitation is inefficiently treated, and that a non-invasive, fast-acting, patient-controlled treatment such as AZ-004 can provide a superior solution — one that allows safe, rapid and effective early intervention before agitation escalates out of control, and provides better emergency treatment for patients whose agitation has reached a crisis.



“Something small can start it. Something inconsequential and out of my control – like a line moving too slowly or a cell phone not working – and this feeling of anxiety and irritation and resentment just takes root and begins growing. It not only takes over my thoughts, it’s also physically uncomfortable.

The feeling builds up inside, sometimes for days. Then, inevitably, it boils over, and I get angry and rude and act in ways that I just can’t stand. And I simply cannot control any of it.

It’s incredibly frustrating.”

— MARC L.  
Individual Living with Bipolar Disorder  
New Jersey —

“Though agitated individuals may seem frightening to other people, they themselves frequently are struggling with overwhelming feelings such as rage, terror and despair. The faster we can help calm their agitation, the more quickly we can remove their fears and anguish, and help make them – and everyone around them – safer.”

— SCOTT ZELLER, MD  
Emergency Psychiatrist  
Partner, JSA Health  
California —



# rapid, non-invasive, reliable relief.

AZ-004 is the only drug to meet all three criteria for optimal treatment of agitation

	AZ-004	Oral Tablet	Rapid Dissolve Tablet	IM Injection
RAPID ONSET OF ACTION	●	—	—	◐
RELIABILITY OF MEDICATION DELIVERY	●	—	◐	●
EASE OF ADMINISTRATION/PATIENT PREFERENCE	●	●	●	—

The American Association of Emergency Psychiatrists has long recognized that there are real challenges when dealing with acute agitation in the clinic. In 2005, the group published "Expert Consensus Guidelines for Treatment of Behavioral Emergencies," which spells out the three primary goals for treating an episode of agitation:

- > rapid onset of therapeutic effect
- > reliable / predictable delivery of medication
- > patient preference for form of treatment

Current standards of care for treating agitation do not meet all three of these criteria. Injections, usually an intramuscular injection of an anti-psychotic or sedative, provide relatively rapid onset and dosing reliability, but are invasive and not preferred by patients — especially in the highly distressed and panicky state typical of agitation episodes. Tablets are simple to administer and are preferred by patients because they are non-invasive, but even rapid-dissolve pills can take too long to begin providing relief to calm agitated patients.

AZ-004 meets all three of the treatment guidelines. With a single, normal breath, the *Staccato*® technology delivers an accurate, rapidly absorbed dose of loxapine via the deep lung. This well studied anti-psychotic drug has excellent receptor binding attributes, a positive side effect profile for acute and intermittent conditions, and has a "calming action" effect that is preferred by clinicians for treating agitation.

Therapeutic effect from AZ-004 is rapid, comparable with an intravenous injection (showing a statistical reduction of agitation in 10 minutes in clinical studies), and agitated patients in clinical trials have found the *Staccato* device to be non-threatening and easy to use. Physicians and nurses have also embraced AZ-004 for its simplicity, speed of onset, and reliability. By allowing agitated patients more control of their treatment, AZ-004 may help clinicians achieve a less threatening atmosphere and greater rapport with agitated patients.

"The successful clinical trials we conducted with AZ-004 underscored a major change to treating agitation in patients who were either bipolar entering manic phase or experiencing early flare-up of schizophrenia symptoms. I personally saw extremely rapid calming effect in both patient populations, and the drug was very safe and well tolerated, while given at 10-20% of the usual dosing for treating agitation.

AZ-004 truly is a 'game-changer' because in my 25 years of clinical trials research I have never seen any medication like this that has such a rapid, yet safe response. I believe *Staccato* is the future of medication delivery for most of the disorders I treat as a neuropsychiatrist."

— MICHAEL LESEM, MD  
Medical Director  
Claghorn-Lesem Research Clinic  
Texas —



"When my brother starts feeling agitation building, it's like a big wave is starting to swell up and up. You know it's building, you know it's hanging over your head, and you know it's going to crash down, but you don't know when or where. And you have **no way of stopping it.** He needs me to

give him a lot of attention and patience to get through an episode so the wave doesn't just overwhelm him. It's a real challenge for both of us every time."

— ROCHELLE R.  
Sister and Caregiver for Chris I.

AND CHRIS I.  
Individual Living with Schizophrenia  
New York —

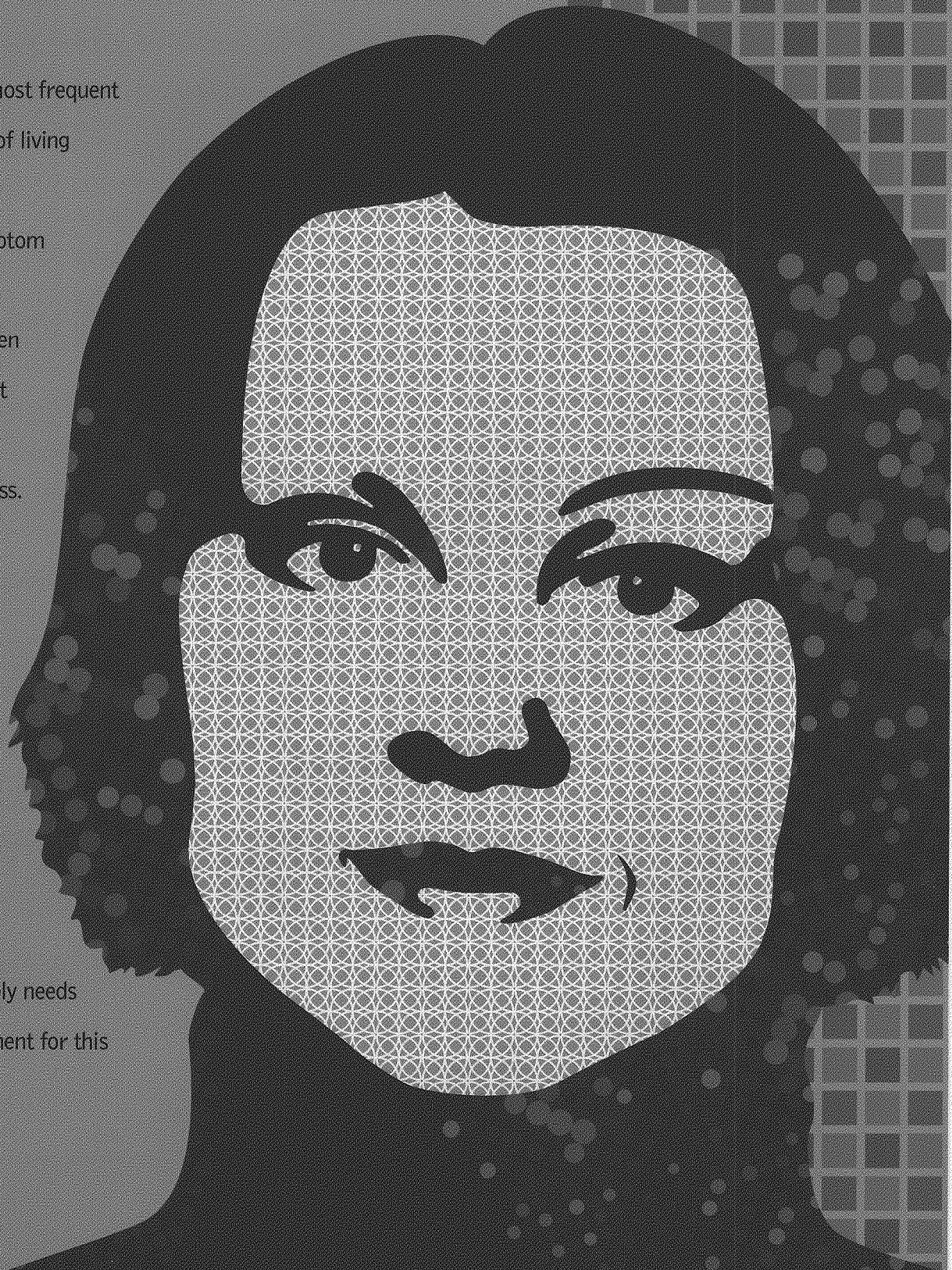




“Agitation is one of the most frequent and frustrating elements of living with bipolar disorder or schizophrenia. It is a symptom of the illness that the individuals themselves often don’t understand, and that instigates feelings of self-hatred and hopelessness. Easing the agitation or at least allowing the people living with schizophrenia or bipolar disorder to manage the condition more effectively would bring a **significant improvement in quality of life.**

This community desperately needs successful forms of treatment for this debilitating symptom.”

— KIM Z.  
Patient Advocate  
Depression and Bipolar Support  
Alliance, NYC Chapter  
New York —





"Biovail is delighted to be working with Alexza to introduce this unique new treatment for agitation. *Staccato* loxapine represents a novel option in the therapeutic armamentarium to treat a condition that can be very stressful for patients and hospital staff alike."

— CHRIS FIBIGER, PhD  
Chief Scientific Officer  
Biovail Laboratories International SRL —

# the *staccato* advantage.

Designed specifically to treat acute and intermittent conditions

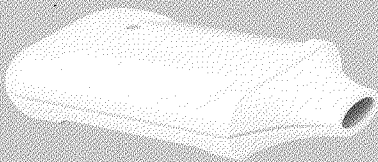
NON-INVASIVE, WITH IV-LIKE KINETICS

NO FORMULATION AND NO EXCIPIENTS OR ADDITIVES

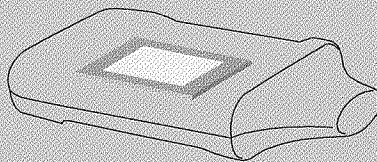
RELIABLE AND CONSISTENTLY HIGH  
EMITTED DOSE (> 80%)

HIGH BIOAVAILABILITY OF EMITTED DOSE (> 90%)

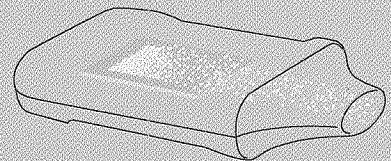
## ALEXZA PROPRIETARY TECHNOLOGY



**THE STACCATO DEVICE**



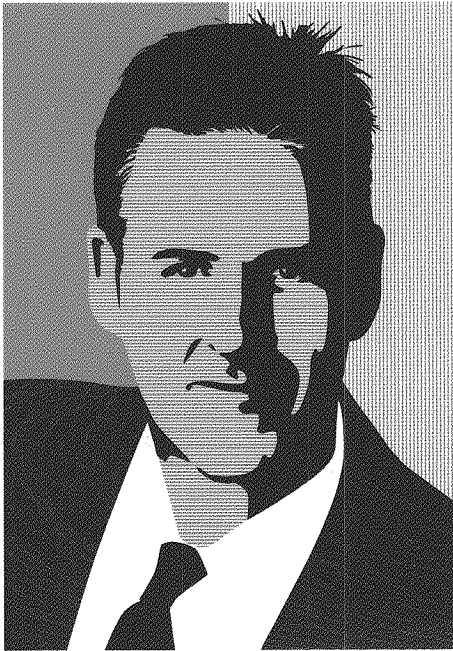
**BEFORE INHALATION:**  
Drug coated on substrate



**DURING INHALATION:**  
The substrate surface instantaneously heats to create perfectly sized particles of excipient-free drug for deep lung delivery

The *Staccato* technology at the core of AZ-004 is a novel form of inhaled drug delivery that is uniquely suited for conditions requiring speed of therapeutic effect, reliable dosing and ease of use. The *Staccato* system single-dose device houses a heat package comprising a stainless steel substrate, which is coated with excipient-free drug — the system requires

no excipients or pharmaceutical stabilizers. With a single breath by the patient, the system rapidly actuates to form a drug aerosol of consistent sized particles between one and three microns. At this size, the particles are rapidly absorbed in the deep lung, ensuring rapid uptake in the bloodstream and rapid onset of pharmacological effect.



“Alexza could have regulatory approval by the end of this year for AZ-004, our first *Staccato*-based product and a new treatment that we believe could substantially improve the lives of those experiencing agitation.”

**TO OUR STOCKHOLDERS** 2009 was a pivotal and successful year for Alexza Pharmaceuticals. After reporting in late 2008 that our lead product candidate AZ-004 (*Staccato* loxapine) had generated highly significant Phase 3 trial results in two clinical trials as a rapid treatment of agitation in patients with schizophrenia or bipolar disease, we spent the better part of 2009 preparing our first New Drug Application. Filing an NDA is a landmark event for any company, and especially for a small company, as we filed our first submission for a new product on a new technology.

It is a testament to the expertise, focus and extraordinary commitment of everyone at Alexza that we submitted the AZ-004 NDA ahead of schedule on December 11, 2009. The FDA has indicated a Prescription Drug User Fee Act (PDUFA) goal date of October 11, 2010, meaning that if all goes well, Alexza could have regulatory approval by the end of this year for our first *Staccato*-based product — a product that we believe could substantially improve the lives of those experiencing and treating agitation.

It is further testament to the creativity and hard work of everyone at Alexza — and to the substantial utility of AZ-004 as a novel and potentially superior treatment for agitation in patients with schizophrenia and bipolar disorder — that in early 2010 we announced a collaboration with Biovail Laboratories to develop and commercialize AZ-004 for the initial indication, as well as possible additional indications in the future. Under the terms of the collaboration, Alexza received an upfront cash payment of \$40 million and may receive up to \$90 million in future potential milestone payments. During our evaluation of possible partners for AZ-004, Biovail stood out as being uniquely suited for AZ-004 — and for Alexza. Biovail is a strong, well-regarded specialty pharmaceutical company, has set a strategic goal of becoming a leader in niche CNS drugs and is highly motivated to utilize AZ-004 as a key stepping stone to their long-term success. We feel Biovail is an excellent choice for the commercialization of AZ-004 in the United States and Canada.

In 2009, Alexza has turned a corner — we have transitioned steadily and efficiently from a development-focused company to a pre-commercial entity preparing and filing our first NDA, continuing the scale-up of our commercial manufacturing and preparing for our first product launch. We have been evolving toward this for some time.

**PROGRESS IN A DIFFICULT ENVIRONMENT** The general economic and financial market decline of the past 18 months created challenges for all companies and particularly for those in capital-intensive industries such as new drug development. Alexza responded by aggressively streamlining its operations and strengthening its balance sheet. Early in 2009, we reduced our workforce by more than 30% and suspended funding of all non-partnered product development programs in our pipeline other than AZ-004 and AZ-104. As a result, throughout the year we put a very large effort into the continued rapid development of AZ-004, including five follow-on trials that we successfully completed, a pre-NDA meeting with the FDA in July, and finalizing our first commercial collaboration for AZ-004 in early 2010.

In June, we announced that we renegotiated and exercised our option to purchase all the equity of Symphony Allegro. By doing so, we regained full ownership of the three product candidates that had been partially funded by Symphony. Under the terms of our Symphony Allegro purchase, Symphony Capital and its affiliates now own approximately

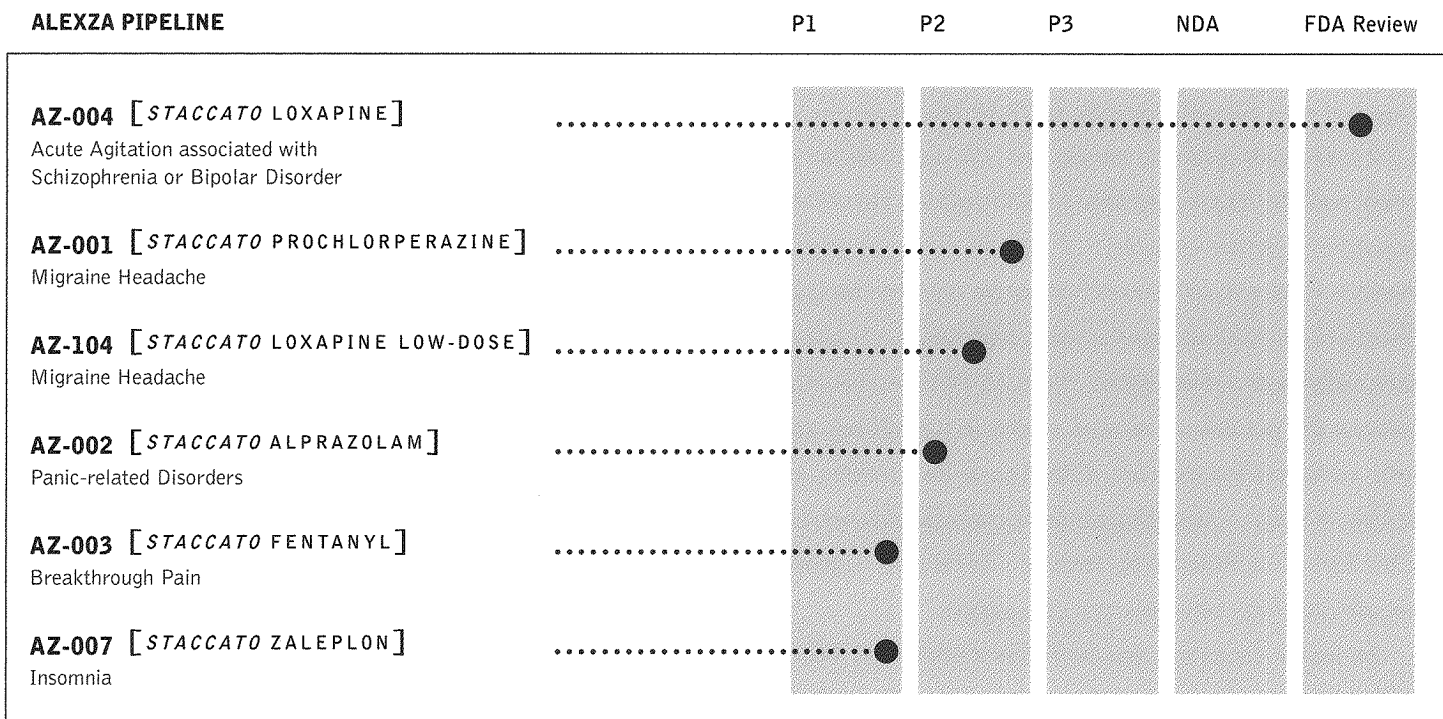
12% of Alexza common stock. We were also pleased to welcome Andy Busser, a partner and co-founder of Symphony Capital, to the Alexza Board of Directors.

Also during 2009, we further bolstered our balance sheet by completing a \$19.7 million private placement of Alexza common stock in early October. We ended the year with cash and equivalents of \$19.9 million. With the cash generated from the upfront payment associated with our collaboration with Biovail, along with the additional milestones that we believe are possible in the next 12 months, we feel Alexza is well positioned financially to support the AZ-004 NDA review, the anticipated launch of AZ-004 and beyond.

**PROMISING PRODUCT/PROMISING MARKET** Our optimism about AZ-004 is based on two factors. First, we believe the product candidate shows effectiveness in treating agitation, as represented by data from our clinical trials. And second, our primary market research indicates that the patient population suffering agitation is larger than is easily identified and it is currently not well served by existing treatments. There are currently no products approved to treat agitation that are both fast-acting and non-invasive — both key attributes of AZ-004.

As we detailed in last year’s annual report, AZ-004 met both the primary and key secondary endpoints in the two Phase 3 trials treating

**ALEXZA PIPELINE**



“We have established a mutually beneficial collaboration with Biovail Laboratories to commercialize AZ-004 for agitation, as well as possible additional indications in the future.”

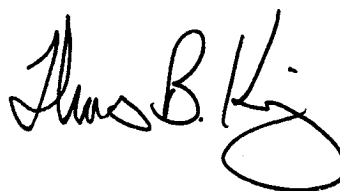
agitation in patients with schizophrenia and bipolar disorder. Both trials enrolled and were completed quickly, which we believe demonstrates how enthusiastically patients, nurses, and clinicians responded to this new tool for treating agitation. Unlike existing modalities — intramuscular injections or tablets — AZ-004 meets the three key attributes in treatment guidelines outlined by the American Association of Emergency Psychiatrists: speed of onset, predictability of medication delivery, and patient preference/ease-of-use. AZ-004 is as non-invasive as taking a pill, but delivers relief as quickly as ten minutes. As the patients, caregivers and clinicians highlighted in the preceding pages make clear, AZ-004 — combining our proprietary *Staccato* technology with the well-characterized drug, loxapine — may offer a genuinely unique and potentially better way to treat agitation.

We believe the patient population that could benefit from this new form of treatment is large. There are 2.4 million adults with schizophrenia and 5.7 million adults with bipolar disorder in the United

States. Our research shows that approximately 90% of them suffer from acute agitation and that those patients average between 11 and 12 agitation episodes every year.

READY FOR THE NEXT STEP Alexza has put the infrastructure in place to serve this market. We have established strong technology and materials supply relationships for our *Staccato* devices and built a cGMP manufacturing facility at our headquarters in Mountain View, California. Our senior management team overseeing regulatory and manufacturing operations is very strong. And with our Biovail collaboration, we have a strong, complementary commercial partner for AZ-004. We feel our relationship will be mutually beneficial and both companies are anticipating a positive decision from the FDA later this year leading to an initial launch of AZ-004 in early 2011.

In closing, let me once again thank Alexza’s stockholders, partners, and especially our employees for your continued support and dedication in a challenging environment. 2010 promises to be another transforming year for the company. We have started with excellent positive momentum and hope to continue that positive trend through the months ahead. I look forward to reporting on our progress.



THOMAS B. KING  
President and Chief Executive Officer  
April 2010

# corporate information

**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 Quality

**Joseph L. Baker**

Vice President  
Commercial Manufacturing

**Robert S. Fishman, MD, FCCP**

Vice President  
Clinical Development

**Emily Lee Kelley, SPHR**

Vice President  
Human Resources

**Christopher Kurtz**

Vice President  
Global Supply Chain and  
Sustainment Engineering

**Peter D. Noymer, PhD**

Vice President  
Product Research and Development

**Mark K. Oki**

Vice President  
Finance and Controller

**Isaac Stein – Lead Director**

President  
Waverly Associates, Inc.

**Hal V. Barron, MD**

Executive Vice President  
Genentech, Inc.  
Chief Medical Officer  
F. Hoffman-La Roche, Ltd.

**Andrew L. Busser**

Partner and Managing Member  
Symphony Capital LLC

**Samuel D. Colella**

Managing Director  
Versant Ventures

**Alan D. Frazier**

General Partner  
Frazier Healthcare Ventures

**Thomas B. King**

President and Chief Executive Officer  
Alexza Pharmaceuticals, Inc.

**Deepika R. Pakianathan, PhD**

General Partner  
Delphi Ventures

**J. Leighton Read, MD**

General Partner  
Alloy Ventures

**Gordon Ringold, PhD**

Chairman and Chief Executive Officer  
Atavita, Inc.

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650.944.7000

Cooley Godward Kronish LLP  
720.566.4000  
www.cooley.com

BNY Mellon Shareowner Services  
877.237.7981  
www.bnymellon.com/shareowner

Ernst & Young LLP  
650.496.1600  
www.ey.com

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](http://www.alexza.com) or write to:

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

The annual meeting of stockholders will be held on Tuesday, May 18, 2010 at 2:30 p.m. California time at the Company's headquarters.

Alexza common stock is traded on the Nasdaq Stock Market under the symbol ALXA. As of December 31, 2009, there were 52,411,356 shares outstanding.

**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, 2009 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.



ALEXZA  
PHARMACEUTICALS

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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 insomnia.

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