# Future in focus

Committed to improving the lives of patients with CNS disorders



ACADIA Pharmaceuticals 2013 Annual Report

### **About ACADIA**

We are a biopharmaceutical company focused on the development and commercialization of innovative medicines that address unmet medical needs in neurological and related central nervous system disorders. We have a pipeline of product candidates led by pimavanserin, which is in Phase III development as a potential first-in-class treatment for Parkinson's disease psychosis. Pimavanserin is also in Phase II development for Alzheimer's disease psychosis and has successfully completed a Phase II trial as a co-therapy for schizophrenia.



### Q. For ACADIA, 2013 was a transformational year. What stands out most?

A. In 2013, we made impressive progress toward our ultimate goal of bringing innovative medicines like pimavanserin, our most advanced product candidate, to market in order to improve the lives of patients with neurological and related central nervous system disorders. Pimavanserin represents a potential new class of psychosis medicine and, we believe, is positioned to be the first drug approved in the United States for the treatment of Parkinson's disease psychosis (PDP). The year was highlighted by several important achievements that fundamentally changed ACADIA.

During the first half of the year, we presented data from our successful pivotal Phase III -020 Study with pimavanserin for PDP at clinical meetings. Importantly, based on the strength of our data, we established an expedited path to registration with the FDA. This may enable pimavanserin to be



Uli Hacksell, Ph.D. Chief Executive Officer

available earlier than previously expected to help Parkinson's patients suffering from psychosis. We also significantly strengthened our financial position through a public stock offering. We followed this with solid performance in the second half of 2013, highlighted by publication of our -020 Study results in *The Lancet*, continued progress in our PDP program, and the initiation of our Phase II trial with pimavanserin in Alzheimer's disease psychosis (ADP). All in all, 2013 was clearly an extraordinary year for ACADIA, and we are focused on building on this momentum during 2014.

### Q. What is Parkinson's disease psychosis (PDP) and how is it treated today?

A. Today about 1 million people in the United States – and from 4 million to 6 million worldwide – suffer from Parkinson's disease. PDP develops in up to 60 percent of patients with Parkinson's disease, commonly causing visual hallucinations and paranoid delusions. This debilitating disorder can have a devastating effect on patients as well as their caregivers and families. Currently, no drug is approved in the United States to treat PDP.

Because there are no other options, physicians frequently resort to off-label use

### Future in focus

Committed to improving the lives of patients with CNS disorders

of antipsychotic drugs, which carry a black box warning in the United States for use in elderly patients with dementia-related psychosis due to increased morbidity and mortality. In addition to safety concerns, physicians face a dilemma because current antipsychotics can worsen the motor control of these patients by counteracting the customary dopamine therapy for Parkinson's disease. Because of its innovative non-dopaminergic mechanism of action, pimavanserin avoids this "dopamine dilemma" and has the potential to be the first safe and effective drug to treat PDP without compromising motor control, thereby significantly improving the quality of life for patients with Parkinson's disease.

## Q. How can pimavanserin for PDP help patients and their caregivers?

A. For both patients and their caregivers, PDP substantially contributes to the burden of Parkinson's disease. It can put tremendous stress on caregivers, often isolating the patient's spouse or other family members. PDP is associated with nursing home placement and increased mortality. We believe that pimavanserin has the ideal profile to address this large unmet medical need by providing the first effective, safe and well-tolerated therapy for PDP. Ultimately, pimavanserin may allow PDP patients to enjoy a better quality of life and stay in their own homes longer.

"Pimavanserin represents a potential new class of psychosis medicine and, we believe, is positioned to be the first drug approved in the United States for the treatment of PDP."

## Q. What are your next steps before filing a New Drug Application (NDA) with the FDA?

A. Our team has been focused on completing the remaining activities in our pimavanserin PDP development program that are needed for submission of an NDA, including aspects of the Chemistry, Manufacturing and Controls (CMC) development and customary supportive studies. We continue to be very pleased with the progress in our PDP program and remain on track for a planned NDA submission near the end of 2014.

## Q. How do you plan to market pimavanserin for PDP in the United States?

A. Our strategy is to commercialize pimavanserin for PDP in the United States by establishing a specialty sales force focused primarily on neurologists.

Already, we have assembled a core commercial organization to help prepare for the planned launch

### Recent ACADIA Milestones

#### March 2013

Presents data from pivotal Phase III -020 Study with pimavanserin in Parkinson's disease psychosis at the American Academy of Neurology 65th Annual Meeting.

#### **April 2013**

Establishes an expedited path to NDA filing for pimavanserin with the FDA.

#### May 2013

Raises \$108 million in public offering of common stock.

#### May 2013

ACADIA is added to NASDAQ Biotechnology Index.

#### June 2013

Advances novel glaucoma compound into preclinical development through Allergan collaboration.



of pimavanserin for our lead indication. This team, led by Terry Moore, our Executive Vice President and Chief Commercial Officer, includes seasoned professionals with extensive experience in marketing, reimbursement and managed markets, commercial operations, and sales force planning and management. They have contributed to building major brands in the CNS field.

To support the planned future U.S. market launch, we continue to conduct extensive market research to optimize the positioning of pimavanserin in the PDP market in order to best serve the needs of prescribers, patients and payers. We also have begun supply chain distribution activities and initial preparations to position us for the larger commercial organization that we plan to have in place at the

time of launch. The more we study the PDP market, the more excited we have become for the potential for pimavanserin to improve the lives of people impacted by this disease.

## Q. Are you looking at broadening the pimavanserin franchise for other indications?

**A.** Yes. We believe that pimavanserin also may be well-suited to address other major neurological and psychiatric disorders, including Alzheimer's disease psychosis (ADP) and schizophrenia, which are poorly served by currently available therapies.

We are excited to have initiated our Phase II ADP trial – an important event because ADP represents such a large unmet medical need. Of the estimated 5.2 million patients in the United States with

#### June 2013

Presents data from Phase III Parkinson's disease psychosis program at the 17th International Congress on Parkinson's Disease and Movement Disorders.

#### June 2013

ACADIA is added to Russell 2000 Index.

#### August 2013

Appoints Terrence Moore as EVP and Chief Commercial Officer.

#### November 2013

Publishes results from pivotal Phase III -020 Study with pimavanserin for Parkinson's disease psychosis in *The Lancet*.

#### November 2013

Initiates Phase II trial with pimavanserin for Alzheimer's disease psychosis.

#### March 2014

Raises \$197 million in public offering of common stock.

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Alzheimer's disease, between 25 percent and 50 percent may develop psychosis. As is the case with PDP, no drug is currently approved in the United States to treat ADP. The off-label use of existing antipsychotics is linked to increased mortality, serious adverse events and cognitive decline in elderly patients with dementia-related psychosis. In addition to ADP, we are actively planning additional studies in our life cycle management program to further characterize potential aspects of pimavanserin's clinical profile and to position it for other indications, including schizophrenia. We believe pimavanserin has multiple applications in this disease area, including the potential to provide a well-tolerated maintenance therapy that may result in better compliance for schizophrenia patients.

## Q. What are the opportunities for pimavanserin outside the United States?

A. ACADIA discovered pimavanserin and holds worldwide commercialization rights to this new chemical entity. We have established a broad patent portfolio, which includes numerous issued patents covering pimavanserin in major markets throughout the world.

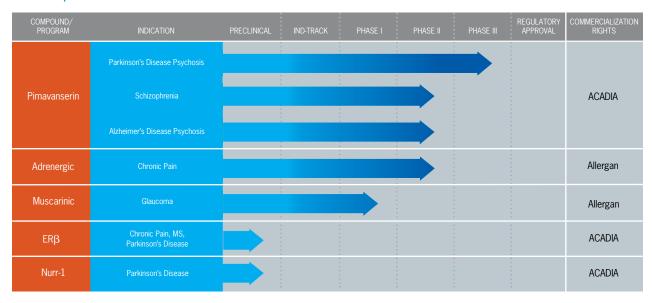
While our focus is clearly on our planned NDA submission in the United States, we also have advanced efforts to outline the path to registration in the European Union. We will also assess the requirements for registration in other key ex-U.S. markets. We may choose to commercialize pimavanserin in selected markets outside the United States through, or in collaboration with, partners.

## Q. Financially, how is ACADIA positioned to advance its pipeline?

A. Today we are well capitalized as we pursue our strategy to build a leading U.S. specialty neurology franchise using pimavanserin as our foundation. We ended 2013 with \$186 million in cash and investment securities, which included net proceeds of \$108 million raised in a public stock offering in May 2013. Following year-end, in March 2014, we significantly bolstered our financial position, raising net proceeds of \$197 million in a public stock offering.

With our strong balance sheet, we believe we are well-positioned to expand the breadth of, and build additional value in, our pimavanserin franchise, and to finance commercial activities. We believe that our

### Our Pipeline



pipeline of product candidates, led by our Phase III pimavanserin program, positions ACADIA with multiple attractive commercial opportunities and significant growth potential.

### Q. What is your long-term strategic vision for ACADIA?

A. Today we are building the foundation to become a leading biopharmaceutical company dedicated to developing and commercializing innovative therapies that improve the lives of patients with neurological and related CNS disorders. As we approach our 10th anniversary as a publicly traded company, we are transforming ACADIA from a discovery and development organization into what we expect will be a successful development and commercial organization. We remain deeply committed to providing important new therapies to patients and delivering value for our stockholders.

#### Q. What excites you most about working at ACADIA?

A. This is an exciting time at ACADIA. For me personally, it is gratifying to see our pimavanserin program advance toward NDA submission this year, which moves us closer to our goal of having this innovative medicine available to patients suffering from PDP. I couldn't be more proud of our growing team of dedicated employees for helping us to deliver on the promise of discoveries that have emanated directly from our internal research. The ultimate reward for all of us at ACADIA is to be part of a team effort that will provide valuable medicine to improve the lives of patients and their caregivers.

Uli Hacksell, Ph.D. Chief Executive Officer April 2014

"We are generally called when the family can no longer cope. They often describe the patient seeing things that are not there, not sleeping, restless and up all night. The family doesn't know what to do as the burden to care for someone 24 hours a day can be totally draining."

—PDP Professional Caregiver, **ACADIA Market Research Study** 

"Parkinson's disease psychosis poses a major challenge because the options to treat the condition are limited and may either compromise patient management of motor symptoms or risk side effects that could be serious for the patient or even increase the risk of death."

—Stuart H. Isaacson, M.D., Director of the Parkinson's Disease and Movement Disorders Center of Boca Raton





At ACADIA, we take pride in developing innovative treatments to address large unmet medical needs in neurological and related central nervous system disorders. We are committed to making a meaningful difference in the lives of patients with CNS disorders and the family members who take care of them every day.

## **ACADIA Pharmaceuticals**

FORM 10-K AND PERFORMANCE MEASUREMENT GRAPH



### UNITED STATES SECURITIES AND EXCHANGE COMMISSION WASHINGTON, D.C. 20549

### Form 10-K

(Mark One)	O SECTION 13 OR 15(d) OF THE				
	04				
For the transition period from to					
Commission File Number: 000-50768					
ACADIA PHARMACEUTICALS INC. (Exact Name of Registrant as Specified in Its Charter)					
Delaware	06-1376651				
(State or Other Jurisdiction of	(I.R.S. Employer				
Incorporation or Organization)	Identification Number)				
11085 Torreyana Road, Suite 100					
San Diego, California	92121				
(Address of Principal Executive Offices)	(Zip Code)				
Registrant's telephone num (858) 558					
Securities registered pursuant Title of each class	to Section 12(b) of the Act:  Name of each exchange on which registered				
Common Stock, par value \$0.0001 per share	The 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 sear					
Indicate by check mark if the registrant is not required to file Exchange Act of 1934. Yes ☐ No ☒					
Indicate by check mark whether the registrant (1) has filed a Securities Exchange Act of 1934 during the preceding 12 months file such reports), and (2) has been subject to such filing requirem	s (or for such shorter period that the registrant was required to nents for the past 90 days. Yes $\boxtimes$ No $\square$				
Indicate by check mark whether the registrant has submitted every Interactive Data File required to be submitted and posted p 12 months (or for such shorter period that the registrant was requ Indicate by check mark if disclosure of delinquent filers pur and will not be contained, to the best of the registrant's knowledg by reference in Part III of this Form 10-K or any amendment to the	ursuant to Rule 405 of Regulation S-T during the preceding ired to submit and post such files). Yes No suant to Item 405 of Regulation S-K is not contained herein, ge, in definitive proxy or information statements incorporated				
Indicate by check mark whether the registrant is a large accessmaller reporting company. See definitions of "large accelerated Rule 12b-2 of the Securities Exchange Act of 1934:	elerated filer, an accelerated filer, a non-accelerated filer, or a filer", "accelerated filer" and "smaller reporting company" in				
Large accelerated filer ⊠	Accelerated filer				
Non-accelerated filer [ ] (Do not check if a smaller reporting	g company) Smaller reporting company				
Indicate by check mark whether the registrant is a shell compact of 1934). Yes $\square$ No $\boxtimes$					
market value of the registrant's common stock held by non-affilia on the closing price of the registrant's common stock on the NAS	SDAQ Global Market on June 28, 2013 of \$18.15 per share.				
As of January 31, 2014, 91,348,503 shares of the registrant' <b>DOCUMENTS INCORPOR</b>					
Portions of the registrant's definitive Proxy Statement to be April 30, 2014 are incorporated by reference into Part III of this in	filed with the Securities and Exchange Commission by				
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#### ACADIA PHARMACEUTICALS INC.

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#### PART I

#### FORWARD-LOOKING STATEMENTS

This report and the information incorporated herein by reference contain forward-looking statements that involve a number of risks and uncertainties, as well as assumptions that, if they never materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements. Although our forward-looking statements reflect the good faith judgment of our management, these statements can only be based on facts and factors currently known by us. Consequently, forward-looking statements are inherently subject to risks and uncertainties, and actual results and outcomes may differ materially from results and outcomes discussed in the forward-looking statements.

Forward-looking statements can be identified by the use of forward-looking words such as "believes," "expects," "hopes," "may," "will," "plans," "intends," "estimates," "could," "should," "would," "continue," "seeks," "aims," "projects," "predicts," "pro forma," "anticipates," "potential" or other similar words (including their use in the negative), or by discussions of future matters such as the development of product candidates or products, technology enhancements, possible changes in legislation, and other statements that are not historical. These statements include but are not limited to statements under the captions "Business," "Risk Factors," and "Management's Discussion and Analysis of Financial Condition and Results of Operations" as well as other sections in this report. You should be aware that the occurrence of any of the events discussed under the caption "Risk Factors" and elsewhere in this report could substantially harm our business, results of operations and financial condition. If any of these events occurs, the trading price of our common stock could decline and you could lose all or a part of the value of your shares of our common stock.

The cautionary statements made in this report are intended to be applicable to all related forward-looking statements wherever they may appear in this report. We urge you not to place undue reliance on these forward-looking statements, which speak only as of the date of this report.

#### Item 1. Business.

#### **Company Overview**

We are a biopharmaceutical company focused on the development and commercialization of innovative small molecule drugs that address unmet medical needs in neurological and related central nervous system disorders. We have a pipeline of product candidates led by pimavanserin, which is in Phase III development as a potential first-in-class treatment for Parkinson's disease psychosis. We have completed a successful pivotal Phase III trial with pimavanserin in patients with Parkinson's disease psychosis and we are planning to submit a New Drug Application, or NDA, to the U.S. Food and Drug Administration, or FDA, for this indication near the end of 2014. Pimavanserin is also in Phase II development for Alzheimer's disease psychosis and has successfully completed a Phase II trial as a co-therapy for schizophrenia. Our pipeline also includes clinical-stage programs for chronic pain and glaucoma in collaboration with Allergan, Inc., and two advanced preclinical programs directed at Parkinson's disease and other neurological disorders. All of our product candidates and programs emanate from internal discoveries.

Our pipeline of product candidates addresses diseases that are not well served by currently available therapies and that represent large potential commercial market opportunities. We believe our product candidates offer innovative therapeutic approaches and may provide significant advantages relative to current therapies. Our pipeline consists of the following product candidates and programs:

#### Pimavanserin

Overview

Pimavanserin is a new chemical entity that we discovered and have advanced to Phase III development, potentially positioning it to be the first drug approved in the United States for the treatment of Parkinson's

disease psychosis. Pimavanserin selectively blocks the activity of a key serotonin receptor that plays an important role in psychosis. We hold worldwide commercialization rights to pimavanserin and have established a broad patent portfolio, which includes numerous issued patents covering this product candidate in the United States, Europe, and several additional countries.

We are pursuing Parkinson's disease psychosis as our lead indication for pimavanserin. We are focused on advancing our Phase III program to registration and, if approved, we intend to commercialize pimavanserin for this indication in the United States by establishing a specialty sales force. Because of its selective mechanism of action and its efficacy and safety profile observed to date in elderly patients with Parkinson's disease psychosis, we believe that pimavanserin also may be well-suited to treat the psychosis associated with a range of other major neurological and psychiatric disorders.

#### Pimavanserin as a Treatment for Parkinson's Disease Psychosis

Parkinson's disease psychosis is a debilitating disorder that develops in up to 60 percent of patients with Parkinson's disease. This disorder, commonly consisting of visual hallucinations and delusions, substantially contributes to the burden of Parkinson's disease and deeply affects the patient's quality of life. Parkinson's disease psychosis is associated with increased caregiver distress and burden, nursing home placement, and increased morbidity and mortality. Currently, no drug is approved to treat Parkinson's disease psychosis in the United States. Pimavanserin provides an innovative, non-dopaminergic approach and, we believe, has the potential to be the first safe and effective drug that will treat Parkinson's disease psychosis without compromising motor control, thereby significantly improving the quality of life for patients with Parkinson's disease.

We have reported successful results from a pivotal Phase III clinical trial, referred to as the -020 Study, evaluating the efficacy, tolerability and safety of pimavanserin in patients with Parkinson's disease psychosis. Pimavanserin met the primary endpoint of the study by demonstrating a highly significant reduction in psychosis. Pimavanserin also met the key secondary endpoint for motoric tolerability. These results were further supported by highly significant improvements in all secondary efficacy measures and by statistically significant benefits in exploratory efficacy measures of nighttime sleep, daytime wakefulness, and caregiver burden. Consistent with previous studies, pimavanserin was safe and well tolerated in this Phase III trial.

Following our successful -020 Study, we met with the FDA and thereafter announced that the agency agreed that the data from the -020 Study, together with supportive data from our other studies with pimavanserin, are sufficient to support the filing of an NDA for the treatment of Parkinson's disease psychosis. We are currently completing the remaining aspects of our development program that are needed for submission of this NDA. Subject to changes that could result from future interactions with the FDA or other developments, we are planning to submit the NDA near the end of 2014.

#### Pimavanserin as a Treatment for Other Neurological and Psychiatric Indications

We intend to use our Phase III Parkinson's disease psychosis program as a foundation to develop and commercialize pimavanserin for additional neurological and psychiatric indications, including Alzheimer's disease psychosis and schizophrenia, that are underserved by currently marketed antipsychotic drugs. Alzheimer's disease psychosis develops in an estimated 25 to 50 percent of patients with Alzheimer's disease and is associated with more rapid cognitive and functional decline and increased institutionalization. Patients with Alzheimer's disease psychosis and Parkinson's disease psychosis share many characteristics and often exhibit similar psychiatric symptoms. No drug is currently approved in the United States to treat Alzheimer's disease psychosis and the off-label use of current antipsychotics is linked to increased mortality, serious adverse events, and cognitive decline in elderly patients with dementia-related psychosis. We are currently conducting a Phase II trial to examine the efficacy and safety of pimavanserin as a treatment for patients with Alzheimer's disease psychosis. We believe that pimavanserin may be ideally suited to address the need for a new treatment for Alzheimer's disease psychosis that is safe, effective, and well tolerated.

For schizophrenia, current drugs used to treat this disease have substantial limitations, including a range of side effects and inadequate efficacy. We have completed a successful Phase II trial that demonstrated several advantages of co-therapy with pimavanserin and a low, sub-therapeutic dose of risperidone, a commonly prescribed antipsychotic drug. We believe that pimavanserin may be used to provide an improved therapy for patients with schizophrenia and we are currently planning additional studies for this indication.

Alpha Adrenergic Program. In collaboration with Allergan, we have discovered small molecule product candidates for the treatment of chronic pain. Chronic pain is a common form of persistent pain that may be related to a number of medical conditions and is often resistant to treatment. Allergan has conducted several Phase II trials in this program and has reported preliminary results, including positive proof-of-concept in a human visceral pain trial and efficacy signals in two chronic pain trials in the areas of fibromyalgia and irritable bowel syndrome. Allergan has announced that it is seeking a partner for the further development of this program and for commercialization in areas predominantly served by general practitioners.

*Muscarinic Program*. We have discovered and, in collaboration with Allergan, are developing small molecule product candidates for the treatment of glaucoma. Glaucoma is a chronic eye disease and is the second leading cause of blindness in the world. Our selective muscarinic agonists have demonstrated a promising preclinical profile, including robust efficacy and a long duration of action. This program has reached Phase I development.

*ER-Beta Program*. We have discovered a compound that exhibits anti-inflammatory and neuroprotective properties in preclinical models and may have the ability to slow down the progression of Parkinson's disease. This compound also may address symptoms of chronic, inflammatory and neuropathic pain, and may serve as a new approach to the treatment of neurodegeneration associated with multiple sclerosis. We are currently pursuing research and development in this program pursuant to a grant from the National Institute of Neurological Disorders and Stroke, a division of the National Institutes of Health, and through funding from Fast Forward, LLC, and EMD Serono, a subsidiary of Merck KGaA.

**Nurr-1 Program.** We have discovered that low doses of a currently marketed drug, which is used in the treatment of cancer, activate Nurr1-RXR complexes and promote viability of dopamine-containing neurons in preclinical models. We have conducted studies to examine the effect of this compound on neuroprotection and neurodegeneration in preclinical models of Parkinson's disease pursuant to a grant from The Michael J. Fox Foundation. We believe that our Nurr-1 program provides the potential for an innovative disease-modifying therapy for treating Parkinson's disease and other neurological disorders.

We have assembled a management team with significant industry experience to lead the discovery, development, and commercialization of our product candidates. We complement our management team with scientific and clinical advisors, including recognized experts in the fields of Parkinson's disease psychosis, Alzheimer's disease, schizophrenia, and other central nervous system disorders.

"ACADIA" and "R-SAT" are our registered trademarks. Our logos and trademarks are the property of ACADIA Pharmaceuticals Inc. All other brand names or trademarks appearing in this report are the property of their respective holders. Use or display by us of other parties' trademarks, trade dress, or products in this report is not intended to, and does not, imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owners.

We maintain a website at www.acadia-pharm.com, to which we regularly post copies of our press releases as well as additional information about us. Our filings with the Securities and Exchange Commission, or SEC, are available free of charge through our website as soon as reasonably practicable after being electronically filed with or furnished to the SEC. Interested persons can subscribe on our website to email alerts that are sent automatically when we issue press releases, file our reports with the SEC or post certain other information to our website. Information contained in our website does not constitute a part of this report or our other filings with the SEC.

#### **Our Strategy**

Our goal is to discover, develop, and commercialize innovative small molecule drugs that address unmet medical needs in neurological and related central nervous system disorders. Key elements of our strategy are to:

- Develop and commercialize our lead product candidate, pimavanserin, for Parkinson's disease psychosis. We are pursuing Parkinson's disease psychosis as our lead indication for pimavanserin and we are focused on advancing our Phase III program to registration for this indication. We intend to position pimavanserin as a first-in-class treatment for patients with Parkinson's disease psychosis. If approved, we plan to commercialize pimavanserin for this indication in the United States by establishing a specialty sales force focused primarily on neurologists. Outside of the United States, we may choose to commercialize pimavanserin in selected markets by establishing one or more strategic alliances.
- Maximize the commercial potential of pimavanserin by expanding to additional neurological and psychiatric disorders. We intend to use our Phase III Parkinson's disease psychosis program as a foundation to develop and commercialize pimavanserin for additional neurological and psychiatric indications that are underserved by currently available antipsychotics and represent large unmet medical needs. Currently, we are in Phase II development with pimavanserin as a treatment for Alzheimer's disease psychosis. In addition, we have completed a Phase II study in schizophrenia and we are planning additional studies for this indication. We plan to retain commercialization rights in therapeutic areas where we feel pimavanserin can be sold by a specialty sales force that calls on a focused group of physicians. In therapeutic areas that require large specialty or primary care sales forces, we may elect to conduct commercialization through, or in collaboration with, partners.
- Continue to develop our other product candidates for the treatment of central nervous system and
  related disorders. We plan to continue developing our other product candidates, including our
  collaborative programs with Allergan, and our internal preclinical programs. While our resources are
  currently focused on our most advanced product candidates, most notably pimavanserin, we expect to
  pursue additional product candidates in the future. These may be directed at neurological and related
  central nervous system disorders and may be developed independently or in partnerships. We believe
  that a diversified pipeline will mitigate risks inherent in drug development and increase the likelihood of
  commercial success.
- Seek to in-license or acquire complementary products or product candidates. Although all of the product candidates currently in our pipeline emanate from internal discoveries, in the future we plan to in-license or acquire assets, which may include clinical-stage product candidates or products, to augment our pipeline and to leverage the sales force that we intend to establish in the future.

#### **Disease and Market Overview**

Our product candidates address diseases that are not well served by currently available therapies and that represent large potential commercial market opportunities. Background information on the diseases and related commercial markets that may be addressed by our product candidates is set forth below.

#### Parkinson's Disease Psychosis

Parkinson's disease is a chronic and progressive neurodegenerative disorder that involves malfunction and death of nerve cells, or neurons, in a region of the brain that controls movement. This neurodegeneration creates a shortage of an important brain signaling chemical, or neurotransmitter, known as dopamine, thereby rendering patients unable to direct or control their movements in a normal manner. Parkinson's disease is characterized by well-known motor symptoms including tremors, limb stiffness, slowness of movements, and difficulties with posture and balance, as well as by non-motor symptoms, which often include psychosis. Parkinson's disease progresses slowly in most people and the severity of symptoms tends to worsen over time.

Parkinson's disease is the second most common neurodegenerative disorder after Alzheimer's disease. According to the National Parkinson Foundation, about one million people in the United States and from four to six million people worldwide suffer from this disease. Parkinson's disease is more common in people over 60 years of age and the prevalence of this disease is expected to increase significantly as the population ages. Parkinson's disease patients are often treated with dopamine replacement therapies such as levodopa, commonly referred to as L-dopa, which is metabolized to dopamine, and dopamine agonists, which are molecules that mimic the action of dopamine.

Studies have suggested that up to 60 percent of patients with Parkinson's disease will develop Parkinson's disease psychosis, which is a debilitating disorder commonly characterized by visual hallucinations and delusions. The development of psychosis in patients with Parkinson's disease substantially contributes to the burden of Parkinson's disease and deeply affects their quality of life. Parkinson's disease psychosis is associated with increased caregiver stress and burden, nursing home placement, and increased morbidity and mortality.

Treatment of Parkinson's disease psychosis poses a challenge to physicians. The FDA has not approved any drug to treat Parkinson's disease psychosis. Traditionally, there are two approaches that may be applied in the treatment of this condition. Initially, physicians may attempt to decrease the dose of or withdraw the dopamine replacement drugs that are administered to manage the motor symptoms of Parkinson's disease. However, this approach is generally not effective in alleviating psychotic symptoms and often comes at the cost of significant worsening of motor function. Therefore, despite substantial limitations, physicians frequently resort to off-label use of currently marketed antipsychotic drugs, including Seroquel and clozapine, to treat patients with Parkinson's disease psychosis. Due to their dopamine blocking properties, currently marketed antipsychotic drugs may counteract the dopamine replacement therapy and, therefore, often worsen motor symptoms in patients with Parkinson's disease. These drugs also are associated with a number of side effects, which can be especially problematic for elderly patients with Parkinson's disease. In addition, all current antipsychotic drugs have a black box warning for use in elderly patients with dementia-related psychosis due to increased mortality and morbidity.

The only currently marketed antipsychotic drug that has demonstrated efficacy in reducing psychosis in patients with Parkinson's disease without further impairing motor function is clozapine when given at low doses. Studies suggest that this unique clinical utility of low-dose clozapine arises from its potent blocking of a key serotonin receptor, a protein that responds to the neurotransmitter serotonin, known as the 5-HT2A receptor. The use of low-dose clozapine has been approved in Europe, but not in the United States, for the treatment of psychotic disorders in Parkinson's disease. However, routine use of clozapine is limited by safety concerns, including its potential to cause a rare, and potentially fatal, blood disorder that necessitates stringent blood monitoring. Currently, there is a large unmet medical need for new therapies that will effectively treat psychosis in patients with Parkinson's disease without compromising motor control or causing other serious side effects in this elderly and fragile patient population.

#### Alzheimer's Disease Psychosis

Alzheimer's disease is a progressive neurodegenerative disorder that attacks the brain's neurons resulting in the loss of memory, thinking and language skills, and behavioral changes. Its symptoms include cognitive dysfunction, memory abnormalities, progressive impairment in activities of daily living, and a host of behavioral and neuropsychiatric symptoms. Alzheimer's disease primarily affects older people and, in most cases, symptoms first appear after age 60. Alzheimer's disease gets worse over time and is fatal.

According to the Alzheimer's Association, an estimated 5.2 million people in the United States have Alzheimer's disease and it is currently the fifth leading cause of death for people age 65 and older. While diagnostic criteria for Alzheimer's disease mostly focus on the related cognitive deficits, it is often the behavioral and psychiatric symptoms that are most troublesome for caregivers and lead to poor quality of life for patients. These symptoms include agitation, aggressive behaviors, and psychosis. Studies have suggested that

approximately 25 to 50 percent of Alzheimer's disease patients may develop psychosis, commonly consisting of hallucinations and delusions. The diagnosis of Alzheimer's disease psychosis is associated with more rapid cognitive and functional decline and increased institutionalization.

The FDA has not approved any drug to treat Alzheimer's disease psychosis. As symptoms progress and become more severe, physicians often resort to off-label use of antipsychotic medications in these patients. Current antipsychotic drugs are associated with a number of side effects, which can be problematic for elderly patients with Alzheimer's disease. In addition, antipsychotic drugs may exacerbate the cognitive disturbances associated with Alzheimer's disease. Current antipsychotic drugs also have a black box warning for use in elderly patients with dementia-related psychosis due to increased mortality and morbidity. There is a large unmet medical need for a safe and effective therapy to treat the psychosis in patients with Alzheimer's disease.

#### Schizophrenia

Schizophrenia is a severe chronic mental illness that involves disturbances in cognition, perception, emotion, and other aspects of behavior. The positive symptoms of schizophrenia include hallucinations and delusions, while the negative symptoms may manifest as loss of interest and emotional withdrawal. Schizophrenia is associated with persistent impairment of a patient's social functioning and productivity. Cognitive disturbances often prevent patients with schizophrenia from readjusting to society. As a result, patients with schizophrenia are normally required to be under medical care for their entire lives.

According to the National Institute of Mental Health, approximately one percent of the U.S. population suffers from schizophrenia. Worldwide sales of antipsychotic drugs used to treat schizophrenia and other psychiatric conditions were approximately \$23 billion in 2012. These drugs increasingly have been used by physicians to address a range of disorders in addition to schizophrenia, including bipolar disorder and a variety of psychoses and related conditions in elderly patients. Despite their commercial success, current antipsychotic drugs have substantial limitations, including inadequate efficacy and severe side effects.

The first-generation, or typical, antipsychotics that were introduced in the late-1950s block dopamine receptors. While typical antipsychotics are effective against positive symptoms of schizophrenia in many patients, these drugs often induce disabling motor disturbances, and they fail to address or can worsen most of the negative symptoms and cognitive disturbances associated with schizophrenia.

Most schizophrenia patients in the United States today are treated with second-generation, or atypical, antipsychotics, which induce fewer motor disturbances than typical antipsychotics, but still fail to address most of the negative symptoms of schizophrenia. In addition, currently prescribed treatments do not effectively address or may exacerbate cognitive disturbances associated with schizophrenia. It is believed that the efficacy of atypical antipsychotics is due to their interactions with dopamine and 5-HT2A receptors. The side effects induced by the atypical agents may include weight gain, non-insulin dependent (type II) diabetes, cardiovascular side effects, sleep disturbances, and motor disturbances. We believe that these side effects generally arise either from non-essential receptor interactions or from excessive dopamine blockade.

The limitations of currently available antipsychotics result in poor patient compliance. A study conducted by the National Institute of Mental Health, which was published in *The New England Journal of Medicine* in September 2005, found that 74 percent of patients taking typical or atypical antipsychotics discontinued treatment within 18 months because of side effects or lack of efficacy. We believe there is a large unmet medical need for new therapies that have improved side effect and efficacy profiles.

#### Chronic Pain

Chronic pain is a common form of pain that persists or progresses over a long period of time. In contrast to acute pain that usually arises suddenly in response to an identifiable injury and is transient, chronic pain persists

over time and is often resistant to medical treatments. Chronic pain may be related to a number of different medical conditions, including diabetes, arthritis, migraine, fibromyalgia, irritable bowel syndrome, cancer, shingles, and previous trauma or injury.

Fibromyalgia is a common and complex type of chronic pain characterized by chronic widespread muscle pain, stiffness and tenderness of muscles, tendons and joints without detectable inflammation. It also is often associated with fatigue, sleep disorders, anxiety, depression and disturbances in bowel function. Fibromyalgia affects an estimated 12 million people in the United States, predominately women, and is commonly diagnosed in people between the ages of 20 and 50. Irritable bowel syndrome is one of the most common ailments of the intestines and affects an estimated 15 percent of the U.S. population. Common symptoms of irritable bowel syndrome include abdominal pain or discomfort often reported as cramping, bloating, gas, diarrhea and/or constipation.

There are a variety of drugs used to treat patients with chronic pain, including anticonvulsants, selective serotonin and norepinephrine reuptake inhibitors, or SNRIs, tricyclic antidepressants, opioid painkillers, non-steroidal anti-inflammatory agents, and drugs directed at symptoms of irritable bowel syndrome. Currently, the leading chronic pain drugs include Lyrica, an anticonvulsant approved for postherpetic neuralgia, diabetic neuropathic pain and fibromyalgia, and Cymbalta, an SNRI indicated for treatment of diabetic peripheral neuropathic pain, fibromyalgia, and major depressive disorder. Lyrica and Cymbalta had worldwide sales of \$4.6 billion and \$5.1 billion, respectively, in 2013. Cymbalta lost its U.S. patent exclusivity in December 2013.

Only a portion of patients with chronic pain get meaningful relief from anticonvulsants and antidepressants. Side effects of anticonvulsants may include dizziness, somnolence, dry mouth, blurred vision, weight gain, and concentration or attention difficulties. Side effects of SNRIs may include nausea, vomiting, dizziness, sleep disturbances, constipation, dry mouth, anxiety, abnormal vision, headache and sexual dysfunction. Tricyclic antidepressants may have pain-relieving effects in some patients. Common side effects of these agents include dry mouth, blurred vision, and constipation, difficulty with urination, impaired thinking and tiredness. Drugs such as opioid painkillers and non-steroidal anti-inflammatory agents that are effective in treating inflammatory and acute pain usually are not effective in treating chronic pain. Opioid painkillers also have significant side effects that limit their usefulness, and prolonged use of these drugs can lead to the need for increasing dosage and potentially to addiction.

Due to these shortcomings of current therapies, we believe that there is a large unmet medical need for new chronic pain therapies with improved efficacy and side effect profiles.

#### Glaucoma

Glaucoma is a chronic eye disease that, if left untreated, can lead to blindness. According to the World Health Organization, glaucoma is the second leading cause of blindness in the world. Loss of vision is caused by degeneration of the optic nerve, which is responsible for carrying images from the eye to the brain. A frequent symptom of glaucoma is increased fluid pressure within the eye, referred to as intraocular pressure. In the early stages of the disease, there may be no symptoms. It is estimated that over four million people in the United States have glaucoma but only half of those know they have it. Older people are at a higher risk for glaucoma and the disease is more common in people over 60 years of age. The prevalence of glaucoma is expected to increase as the average age of the population increases.

Currently there are a variety of options available to treat glaucoma, including eye medications, laser procedures, and surgery. These treatment options are intended to decrease intraocular pressure and, thereby, protect the optic nerve. Physicians often treat glaucoma with multiple classes of drugs to optimize therapy and minimize side effects. Drugs used to treat glaucoma include two leading prostaglandin analogs, Xalatan and Lumigan, beta blockers such as timolol, and alpha agonists such as Alphagan, as well as combined medications. Worldwide sales of Xalatan, which is now generic, and Lumigan franchises totaled \$589 million and \$625

million, respectively, in 2013. While Xalatan and Lumigan are effective anti-glaucoma agents, these drugs may cause several side effects. Xalatan frequently causes increased darkening, or pigmentation, of the iris that may lead to a change in iris color and may cause other side effects, including blurred vision and burning and stinging sensations in the eye. Side effects of Lumigan may include pigmentation of eye color, eyelid skin and eyelashes, as well as eyelash changes, eye redness, and itchy eyes. We believe there is a need for new treatments with enhanced efficacy that can treat glaucoma with fewer side effects.

#### **Our Product Candidates and Programs**

Our pipeline includes product candidates in clinical development and programs in advanced preclinical testing. We believe that our product candidates offer innovative therapeutic approaches and may provide significant advantages relative to current therapies. The following table summarizes our product candidates and programs:

Product Candidate/Program	Indication	Stage of Development (1)	<b>Commercialization Rights</b>
Pimavanserin	Parkinson's disease psychosis	Phase III	ACADIA
	Alzheimer's disease psychosis	Phase II	ACADIA
	Schizophrenia	Phase II	ACADIA
Alpha adrenergic program	Chronic pain	Phase II	Allergan
Muscarinic program	Glaucoma	Phase I	Allergan
ER-Beta program	Chronic pain, Multiple Sclerosis, Parkinson's disease	Preclinical	ACADIA
Nurr-1 program	Parkinson's disease	Preclinical	ACADIA

<sup>(1)</sup> Stage of development refers to the most advanced stage reached in which development studies have been conducted or are currently in process.

#### **Pimavanserin**

#### Overview

Pimavanserin is a new chemical entity that we discovered and have advanced to Phase III development, potentially positioning it to be the first drug approved in the United States for the treatment of Parkinson's disease psychosis. Pimavanserin is a small molecule that is formulated as a tablet and can be taken orally once-aday. Pimavanserin selectively blocks the activity of the 5-HT2A receptor, a drug target that plays an important role in psychosis. We hold worldwide rights to pimavanserin and have established a patent portfolio, which includes numerous issued patents covering pimavanserin in the United States, Europe, and several additional countries.

We are pursuing Parkinson's disease psychosis as our lead indication for pimavanserin and we are focused on advancing our Phase III program to registration for this indication. We believe that pimavanserin also has the potential to address a range of other neurological and psychiatric indications that are underserved by currently marketed antipsychotics. As part of our life cycle program, we are currently conducting a Phase II trial to evaluate pimavanserin as a treatment for Alzheimer's disease psychosis. In addition, we have completed a Phase II trial with pimavanserin as a co-therapy in schizophrenia and we are planning additional studies for this indication. We intend to use our Phase III Parkinson's disease psychosis program as a foundation to develop and commercialize pimavanserin for these and potentially other neurological and psychiatric indications.

#### Pimavanserin as a Treatment for Parkinson's Disease Psychosis

We are in Phase III development with pimavanserin as a potential first-in-class treatment for Parkinson's disease psychosis. Currently, there are no drugs approved to treat this disorder in the United States. Pimavanserin offers an innovative, non-dopaminergic approach to treating Parkinson's disease psychosis. We believe that pimavanserin has the potential to be the first effective and safe drug that will treat the psychosis in patients with Parkinson's disease without compromising motor control, thereby significantly improving the quality of life for these patients. As a result, we believe that, if approved, pimavanserin will offer significant advantages relative to current antipsychotics used off-label for the treatment of Parkinson's disease psychosis.

In November 2012, we announced successful top-line results from our pivotal Phase III -020 Study, evaluating the efficacy, tolerability, and safety of pimavanserin in patients with Parkinson's disease psychosis. Results from the -020 Study were presented at the American Academy of Neurology Meeting in March 2013, and published in The Lancet, a peer-reviewed medical journal, in November 2013. The -020 Study was a multicenter, double-blind, placebo-controlled clinical trial. A total of 199 patients were enrolled in the study and randomized on a one-to-one basis to receive either 40 mg of pimavanserin or placebo once-daily for six weeks, following a two-week screening period that included brief psycho-social therapy. Patients also received stable doses of their existing anti-Parkinson's therapy throughout the study. Pimavanserin met the primary endpoint in the -020 Study by demonstrating a highly significant reduction in psychosis (p=0.001) as measured using the SAPS-PD, a scale consisting of nine items from the hallucinations and delusions domains of the Scale for the Assessment of Positive Symptoms. Pimavanserin also met the key secondary endpoint for motoric tolerability as measured using Parts II and III of the Unified Parkinson's Disease Rating Scale, or UPDRS. These results were further supported by highly significant improvements in all secondary efficacy measures, including the Clinical Global Impression Severity, or CGI-S scale (p<0.001), the Clinical Global Impression Improvement, or CGI-I scale (p=0.001), and a CGI-I responder analyses (p=0.002). In addition, statistically significant benefits were observed in exploratory efficacy measures of nighttime sleep, daytime wakefulness and caregiver burden. Consistent with previous studies, pimavanserin was safe and well tolerated in this Phase III trial.

Following our successful -020 Study, in April 2013 we met with the FDA and announced that the agency agreed that the data from our -020 Study, together with supportive data from our other studies with pimavanserin, are sufficient to support the filing of an NDA for the treatment of Parkinson's disease psychosis. We are currently completing the remaining aspects of our development program that are needed for submission of this NDA. These include Chemistry, Manufacturing and Controls, or CMC, development, such as stability testing of registration batches, and customary supportive studies, such as drug-drug interaction studies. We also are continuing to conduct our open-label safety extension trial, referred to as the -015 Study, involving patients with Parkinson's disease psychosis who have completed the -020 Study and our earlier Phase III studies. The -015 Study, together with a similar extension trial from our earlier Phase II Parkinson's disease psychosis trial, has generated a considerable amount of long-term safety data on pimavanserin. A total of over 200 patients have been treated with pimavanserin for over one year and our longest single-patient exposure is greater than eight years. We believe that our experience to date suggests that long-term administration of pimavanserin is generally safe and well tolerated in this elderly and fragile patient population.

Subject to changes that could result from future interactions with the FDA or other developments, we are planning an NDA submission near the end of 2014. While the FDA has agreed to accept and review an NDA for pimavanserin on the basis of our positive pivotal -020 Study data, along with supportive efficacy and safety data from other pimavanserin studies, the NDA will be subject to standard FDA review to determine whether the filing package is adequate to support approval for Parkinson's disease psychosis.

#### Pimavanserin as a Treatment for Alzheimer's Disease Psychosis

We are in Phase II development with pimavanserin as a potential new treatment for Alzheimer's disease psychosis. Patients with Alzheimer's disease psychosis and Parkinson's disease psychosis share many characteristics and often exhibit similar psychiatric symptoms associated with their respective underlying

neurodegenerative disease. We have shown that pimavanserin attenuates psychosis-related behaviors in preclinical models of Alzheimer's disease psychosis. In preclinical models, pimavanserin also has been shown to positively interact with cholinesterase inhibitors to enhance their pro-cognitive effect. Because of its selective mechanism of action and its efficacy and safety profile observed to date in studies conducted in elderly patients with Parkinson's disease psychosis, we believe that pimavanserin also may be ideally suited to address the need for a new treatment for Alzheimer's disease psychosis that is safe, effective, and well tolerated.

In November 2013, we initiated a Phase II trial, referred to as the -019 Study, to examine the efficacy and safety of pimavanserin as a treatment for Alzheimer's disease psychosis. The -019 Study is a randomized, double-blind, placebo-controlled study designed to enroll about 200 patients with Alzheimer's disease psychosis. Following a screening period that includes brief psycho-social therapy, patients will be randomized on a one-to-one basis to receive either 40 mg of pimavanserin or placebo once-daily for twelve weeks. The -019 study will assess several key efficacy endpoints, including use of the Neuropsychiatric Inventory—Nursing Home, or NPI-NH, scale to measure psychosis and other behavioral disorders. Key efficacy endpoints will be based on the change at week 6 from baseline. The study will also assess additional exploratory endpoints, including the cognitive status of patients and the durability of response to pimavanserin, through twelve weeks of therapy.

#### Pimavanserin as a Therapy for Schizophrenia

Pimavanserin's selective blockade of the 5-HT2A receptor may enable it to be used in two different treatment approaches to improve the therapy for patients with schizophrenia. First, pimavanserin may be used as a co-therapy, together with low doses of existing atypical antipsychotic drugs such as risperidone, to obtain a more optimal balance between 5-HT2A receptor blockade and partial dopamine receptor blockade. This co-therapy approach has the potential to result in enhanced efficacy and fewer side effects relative to existing treatments. Second, in the maintenance phase of schizophrenia therapy, we believe that it may be desirable to use a treatment that selectively blocks the 5-HT2A receptor and avoids interaction with dopamine receptors, which may be associated with many of the side effects caused by existing antipsychotic drugs. Therefore, we believe that pimavanserin also may have the potential to be used as a stand-alone treatment to provide a well-tolerated maintenance therapy for schizophrenia patients that results in better compliance compared to existing antipsychotic drugs.

We published results in 2012 from an earlier multi-center, double-blind, placebo-controlled Phase II trial designed to evaluate pimavanserin as a co-therapy in patients with schizophrenia. The trial results showed several advantages of co-therapy with pimavanserin and a 2 mg, or low, dose of risperidone in patients with schizophrenia. These advantages included efficacy comparable to that of a 6 mg, or standard, dose of risperidone, combined with a faster onset of antipsychotic action and an improved side effect profile, including significantly less weight gain, compared to the standard dose of risperidone. We are currently planning additional studies for this indication.

#### Alpha Adrenergic Program

In collaboration with Allergan, we have discovered small molecule product candidates for the treatment of chronic pain. Our novel alpha adrenergic agonists provide pain relief in a range of preclinical models, without the side effects of current pain therapies, including sedation and cardiovascular and respiratory effects.

Allergan has conducted several Phase II trials in this program and has reported preliminary results, including positive proof-of-concept in a visceral pain trial in patients that had hypersensitivity of the esophagus, and efficacy signals in two chronic pain trials in the areas of fibromyalgia and irritable bowel syndrome. Allergan has announced that it is seeking a partner for the further development of this program and for commercialization in areas predominantly served by general practitioners.

#### Muscarinic Program

We have discovered and, in collaboration with Allergan, are developing small molecule product candidates for the treatment of glaucoma. Using our proprietary drug discovery platform, we identified a subtype of the

muscarinic receptors that controls intraocular pressure and discovered lead compounds that selectively activate this target. In preclinical models, our product candidates have demonstrated a promising preclinical profile, including robust efficacy and a long duration of action. This program has reached Phase I development.

#### ER-Beta Program

We have discovered an estrogen receptor-beta agonist that exhibits anti-inflammatory and neuroprotective properties in preclinical models and may have the ability to slow down the progression of Parkinson's disease. This compound also may address symptoms of chronic, inflammatory and neuropathic pain, and may serve as a new approach to the treatment of neurodegeneration associated with multiple sclerosis. We are currently pursuing research and development in this program pursuant to a grant from the National Institute of Neurological Disorders and Stroke, a division of the National Institutes of Health, and through funding from Fast Forward, LLC, and EMD Serono, a subsidiary of Merck KGaA.

#### Nurr-1 Program

We have discovered that low doses of a currently marketed drug, which is used in the treatment of cancer, activate Nurr1-RXR complexes and promote viability of dopamine-containing neurons in preclinical models. We have conducted studies to examine the effect of this compound on neuroprotection and neurodegeneration in preclinical models of Parkinson's disease pursuant to a grant from The Michael J. Fox Foundation. We believe that our Nurr-1 program provides the potential for an innovative disease-modifying therapy for treating Parkinson's disease and other neurological disorders.

#### Our Drug Discovery Platform and Capabilities

#### Our Drug Discovery Approach

All of our product candidates and programs emanate from internal discoveries. We have used our proprietary drug discovery platform to rapidly identify drug-like, small molecule chemistries for a range of drug targets. We believe that our expertise combined with our proprietary platform has allowed us to discover product candidates more efficiently than traditional approaches. Our drug discovery approach is designed to introduce chemistry at an early stage in the drug discovery process and enable selection of the most attractive, drug-like chemistries for desired targets. A key to our discovery approach has been our set of proprietary functional test systems, or assays, that we developed for a large number of targets predominantly in the G-protein coupled receptor and nuclear receptor gene families. We believe that these gene families represent the most relevant and feasible targets for small molecule drug discovery focused on central nervous system indications. We have used our proprietary assays in conjunction with our proprietary receptor selection and amplification technology, a cell-based assay system which we refer to as R-SAT, to validate drug targets, and to discover novel small molecules that are specific for these targets.

#### Collaboration Agreements

Historically, we have been a party to various collaboration agreements with Allergan and other parties to leverage our drug discovery platform and related assets, and to advance development of and commercialize selected product candidates. These collaborations have typically included upfront payments at initiation of the collaboration, research support during the research term, if applicable, milestone payments upon successful completion of specified development objectives, and royalties based upon future sales, if any, of drugs developed under the collaboration. Our current agreements are as follows:

In July 1999, we entered into a collaboration agreement with Allergan to discover, develop and commercialize selective muscarinic drugs for the treatment of glaucoma. Under this agreement, we provided our chemistry and discovery expertise to enable Allergan to select two compounds for development. We granted Allergan exclusive worldwide rights to commercialize products based on these two compounds for the treatment

of ocular disease. As of December 31, 2013, we had received an aggregate of \$9.9 million in payments under the agreement, consisting of upfront fees, research funding and milestone payments. We are eligible to receive up to an aggregate of approximately \$15 million in additional payments per product upon the achievement of development and regulatory milestones as well as royalties on future product sales worldwide, if any. Allergan may terminate this agreement upon 90 days' notice. However, if terminated, Allergan's rights to the selected compounds would revert to us.

In September 1997, we entered into a collaboration agreement with Allergan focused primarily on the discovery and development of new therapeutics for pain and ophthalmic indications. This agreement, as amended, provides for the continued development of product candidates for one target area. We are restricted from conducting competing research in that target area. Pursuant to the agreement, we granted Allergan exclusive worldwide rights to commercialize products resulting from the collaboration. We had received an aggregate of \$10.5 million in payments, consisting of research funding and milestone payments, through December 31, 2013 under this agreement. We are eligible to receive additional milestone payments of up to \$10.0 million in the aggregate upon the achievement of development and regulatory milestones as well as royalties on future product sales worldwide, if any. In connection with the execution of the collaboration agreement in 1997, Allergan made a \$6.0 million equity investment in us.

The general terms of our collaboration agreements with Allergan continue until the later of the expiration of the last to expire patent covering a product licensed under the collaboration and at least 10 years from the date of first commercial sale of a product. In addition, each of our Allergan collaboration agreements includes a research term that is shorter but may be renewed if agreed to by the parties.

#### **Intellectual Property**

We currently hold 49 issued U.S. patents and 238 issued foreign patents. All of these patents originated from us. In addition, we have 15 provisional and utility U.S. patent applications and 70 foreign patent applications.

Patents or other proprietary rights are an essential element of our business. Our strategy is to file patent applications in the United States and any other country that represents an important potential commercial market to us. In addition, we seek to protect our technology, inventions and improvements to inventions that are important to the development of our business. Our patent applications claim proprietary technology, including methods of screening and chemical synthetic methods, novel drug targets and novel compounds identified using our technology.

We also rely upon trade secret rights to protect other technologies that may be used to discover and validate targets and that may be used to identify and develop novel drugs. We protect our trade secrets in part through confidentiality and proprietary information agreements. We have entered into a license agreement, dated as of November 30, 2006, for certain intellectual property rights from the Ipsen Group in order to expand and strengthen the intellectual property portfolio for our serotonin platform, including pimavanserin. We are a party to various other license agreements that give us rights to use certain technologies in our research and development.

#### Pimavanserin

Nineteen U.S. patents have been issued to us that provide protection for pimavanserin, including three that cover the compound generically and 10 that specifically cover pimavanserin, polymorphs thereof, the use thereof for treating Parkinson's disease psychosis, Alzheimer's disease psychosis, schizophrenia, bipolar disorder, Lewy body disease, sleep disorders, and other methods of treatment. These patents also provide protection for certain methods of producing pimavanserin. The pimavanserin specific patent and the Parkinson's disease psychosis treatment patent provide protection until June 2027 and 2026, respectively. The patent that covers polymorphs of

pimavanserin provides protection until June 2028. The patents that cover pimavanserin generically expire in 2021. Our estimation of the above patent terms includes patent term adjustments made by the U.S. Patent and Trademark Office. These patent terms may be subject to change based on new interpretations of the law. We have 55 issued foreign patents that specifically cover pimavanserin, including patents in 39 European countries, Australia, Canada, China, Hong Kong, India, Japan, Mexico, New Zealand, Russia, Singapore and South Africa, which provide patent protection through 2024. We continue to prosecute patent applications directed to pimavanserin and to methods of treating various diseases using pimavanserin, either alone or in combination with other agents, worldwide.

#### Alpha Adrenergic Program

We have not been issued, and are not pursuing, patents covering the compounds being pursued by Allergan under this collaboration as the compounds are covered by Allergan patents.

#### Muscarinic Program

We have two U.S. patents that have been issued to us providing coverage for the compounds covered by our collaboration with Allergan for the treatment of glaucoma. These U.S. patents will expire in 2023. We have 48 issued foreign patents and 14 pending foreign applications that cover these compounds. The issued foreign patents for this program will expire in 2022 and 2025.

#### Other Programs

We have 14 issued U.S. patents and 19 issued foreign patents with claims for other compounds that are at earlier stages of development.

#### Our Drug Discovery Platform

Our core R-SAT technology is protected by eight issued U.S. patents and 17 foreign patents. Our U.S. patents for R-SAT will expire during the period ending 2025. The foreign patents covering R-SAT will expire over the range of 2014 to 2024.

#### Competition

We face, and will continue to face, intense competition from pharmaceutical and biotechnology companies, as well as numerous academic and research institutions and governmental agencies, both in the United States and abroad. We compete, or will compete, with existing and new products being developed by our competitors. Some of these competitors are pursuing the development of pharmaceuticals that target the same diseases and conditions that our research and development programs target.

Even if we and our collaborators are successful in developing our product candidates, the resulting products would compete with a variety of established drugs in the areas of Parkinson's disease psychosis, schizophrenia, Alzheimer's disease psychosis, chronic pain, and glaucoma. For example, pimavanserin for the treatment of Parkinson's disease psychosis will compete with off-label use of antipsychotic drugs, including Seroquel, marketed by Astra-Zeneca, and clozapine, a generic drug.

Our potential products for the treatment of schizophrenia would compete with Zyprexa, marketed by Eli Lilly, Risperdal, marketed by Johnson & Johnson, Abilify, marketed jointly by Bristol-Myers Squibb and Otsuka Pharmaceutical, Seroquel, and clozapine. Zyprexa (olanzapine), Risperdal (risperidone), Seroquel (quetiapine) and clozapine (clozaril) are all now generic in the United States. Our potential product for Alzheimer's disease psychosis would compete with off-label use of antipsychotic drugs.

Our potential products for the treatment of chronic pain would compete with Lyrica, marketed by Pfizer, and Cymbalta, marketed by Eli Lilly, as well as with a variety of generic or proprietary opioids, and other drugs. Currently, the leading drugs approved for chronic pain indications include Lyrica, the successor to Neurontin (gabapentin, now a generic drug), and Cymbalta, now generic in the United States.

Our potential products for the treatment of glaucoma would compete with Xalatan, marketed by Pfizer, and Lumigan and Alphagan, marketed by Allergan. Xalatan (latanoprost) is now generic.

In addition, the companies described above and other competitors may have a variety of drugs in development or awaiting FDA approval that could reach the market and become established before we have a product to sell. Our competitors may also develop alternative therapies that could further limit the market for any drugs that we may develop. Many of our competitors are using technologies or methods different or similar to ours to identify and validate drug targets and to discover novel small molecule drugs. Many of our competitors and their collaborators have significantly greater experience than we do in the following:

- identifying and validating targets;
- · screening compounds against targets;
- preclinical and clinical trials of potential pharmaceutical products; and
- obtaining FDA and other regulatory clearances.

In addition, many of our competitors and their collaborators have substantially greater advantages in the following areas:

- · capital resources;
- research and development resources;
- · manufacturing capabilities; and
- · sales and marketing.

Smaller companies also may prove to be significant competitors, particularly through proprietary research discoveries and collaborative arrangements with large pharmaceutical and established biotechnology companies. Many of our competitors have products that have been approved or are in advanced development. We face competition from other companies, academic institutions, governmental agencies and other public and private research organizations for collaborative arrangements with pharmaceutical and biotechnology companies, in recruiting and retaining highly qualified scientific and management personnel and for licenses to additional technologies. Our competitors, either alone or with their collaborators, may succeed in developing technologies or drugs that are more effective, safer, and more affordable or more easily administered than ours and may achieve patent protection or commercialize drugs sooner than us. Developments by others may render our product candidates or our technologies obsolete. Our failure to compete effectively could have a material adverse affect on our business.

#### **Government Regulation**

The manufacturing and marketing of our potential products and our ongoing research and development activities are subject to extensive regulation by numerous governmental authorities in the United States and other countries. Before marketing in the United States, any new drug developed by us must undergo rigorous preclinical testing, clinical trials and an extensive regulatory clearance process implemented by the FDA under the federal Food, Drug, and Cosmetic Act, as amended. The FDA regulates, among other things, the development, testing, manufacture, safety, efficacy, record keeping, labeling, storage, approval, advertising, promotion, sale and distribution of biopharmaceutical products. None of our product candidates has been approved for sale in the United States or any foreign market. The regulatory review and approval process, which includes preclinical testing and clinical trials of each product candidate, is lengthy, expensive and uncertain. Moreover, if our product candidates are approved by the FDA, government coverage and reimbursement policies

will both directly and indirectly impact our ability to successfully commercialize our products, and such coverage and reimbursement policies will be impacted by future healthcare reform measures. In addition, we may be subject to state and federal laws, including anti-kickback and false claims statutes as well as data privacy laws, which restrict certain business practices in the pharmaceutical industry.

In the United States, product candidates are tested in animals until adequate proof of safety is established. Clinical trials for new product candidates are typically conducted in three sequential phases that may overlap. Phase I trials involve the initial introduction of the product candidate into healthy human volunteers. The emphasis of Phase I trials is on testing for safety or adverse effects, dosage, tolerance, metabolism, distribution, excretion and clinical pharmacology. Phase II involves studies in a limited patient population to determine the initial efficacy of the compound for specific targeted indications, to determine dosage tolerance and optimal dosage and to identify possible adverse side effects and safety risks. Once a compound shows evidence of effectiveness and is found to have an acceptable safety profile in Phase II evaluations, Phase III trials are undertaken to more fully evaluate clinical outcomes. Before commencing clinical investigations in humans, we or our collaborators must submit to the FDA an Investigational New Drug Application, or IND.

Regulatory authorities may require additional data before allowing the clinical studies to commence or proceed from one phase to another, and could demand that the studies be discontinued or suspended at any time if there are significant safety issues. We have in the past and may in the future rely on some of our collaborators to file INDs and generally direct the regulatory approval process for many of our potential products. Clinical testing must also meet requirements for clinical trial registration, institutional review board oversight, informed consent, health information privacy, and good clinical practices.

To establish a new product candidate's safety and efficacy, the FDA requires companies seeking approval to market a drug product to submit extensive preclinical and clinical data, along with other information, for each indication for which the product will be labeled and launched. The data and information are submitted to the FDA in the form of a New Drug Application, or NDA. Generating the required data and information for an NDA takes many years and requires the expenditure of substantial resources. Information generated in this process is susceptible to varying interpretations that could delay, limit or prevent regulatory approval at any stage of the process. The failure to demonstrate adequately the quality, safety and efficacy of a product candidate under development would delay or prevent regulatory approval of the product candidate. We cannot assure you that, even if clinical trials are completed, either our collaborators or we will submit applications for required authorizations to manufacture and/or market potential products or that any such application will be reviewed and approved by the appropriate regulatory authorities in a timely manner, if at all. Under applicable laws and FDA regulations, each NDA submitted for FDA approval is usually given an internal administrative review within 60 days following submission of the NDA. If deemed sufficiently complete to permit a substantive review, the FDA will "file" the NDA. The FDA can refuse to file any NDA that it deems incomplete or not properly reviewable. The FDA has established internal goals of eight months from submission for priority review of NDAs that cover product candidates that offer major advances in treatment or provide a treatment where no adequate therapy exists, and 12 months from submission for the standard review of NDAs. However, the FDA is not legally required to complete its review within these periods, these performance goals may change over time and the review is often extended by FDA requests for additional information or clarification. Moreover, the outcome of the review, even if generally favorable, may not be an actual approval but a "complete response letter" that describes additional work that must be done before the NDA can be approved. Before approving an NDA, the FDA will inspect the facilities at which the product is manufactured and will not approve the product unless the manufacturing facility complies with cGMPs. The FDA's review of an NDA may also involve review and recommendations by an independent FDA advisory committee, particularly for novel indications, such as Parkinson's disease psychosis.

In addition, delays or rejections may be encountered based upon changes in regulatory policy for product approval during the period of product development and regulatory agency review. Changes in regulatory approval policy, regulations or statutes or the process for regulatory review during products' development or approval periods may cause delays in the approval or rejection of an application.

Before receiving FDA approval to market a potential product, we or our collaborators must demonstrate through adequate and well-controlled clinical studies that the potential product is safe and effective on the patient population that will be treated. If regulatory approval of a potential product is granted, this approval will be limited to those disease states and conditions for which the product is approved. Marketing or promoting a drug for an unapproved indication is generally prohibited. Furthermore, FDA approval may entail ongoing requirements for risk management, including post-marketing studies. Even if approval is obtained, a marketed product, its manufacturer and its manufacturing facilities are subject to continuing review and periodic inspections by the FDA. Discovery of previously unknown problems with a product, manufacturer or facility may result in restrictions on the product or manufacturer, including labeling changes, warning letters, costly recalls or withdrawal of the product from the market.

Any drug is likely to produce some toxicities or undesirable side effects in animals and in humans when administered at sufficiently high doses and/or for sufficiently long periods of time. Unacceptable toxicities or side effects may occur at any dose level at any time in the course of studies in animals designed to identify unacceptable effects of a product candidate, known as toxicological studies, or during clinical trials of our potential products. The appearance of any unacceptable toxicity or side effect could cause us or regulatory authorities to interrupt, limit, delay or abort the development of any of our product candidates. Further, such unacceptable toxicity or side effects could ultimately prevent a potential product's approval by the FDA or foreign regulatory authorities for any or all targeted indications or limit any labeling claims, even if the product is approved.

Any trade name that we intend to use for a potential product must be approved by the FDA irrespective of whether we have secured a formal trademark registration from the U.S. Patent and Trademark Office. The FDA conducts a rigorous review of proposed product names, and may reject a product name if it believes that the name inappropriately implies medical claims or if it poses the potential for confusion with other product names. The FDA will not approve a trade name until the NDA for a product is approved. If the FDA determines that the trade names of other products that are approved prior to the approval of our potential products may present a risk of confusion with our proposed trade name, the FDA may elect to not approve our proposed trade name. If our trade name is rejected, we will lose the benefit of any brand equity that may already have been developed for this trade name, as well as the benefit of our existing trademark applications for this trade name. If the FDA does not approve our proposed trade name, we may be required to launch a potential product candidate without a brand name, and our efforts to build a successful brand identity for, and commercialize, this product candidate may be adversely impacted.

We and our collaborators and contract manufacturers also are required to comply with the applicable FDA current good manufacturing practice regulations. Good manufacturing practice regulations include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation. Manufacturing facilities are subject to inspection by the FDA. These facilities must be approved before we can use them in commercial manufacturing of our potential products. The FDA may conclude that we or our collaborators or contract manufacturers are not in compliance with applicable good manufacturing practice requirements and other FDA regulatory requirements.

If the product is approved, we must also comply with post-marketing requirements, including, but not limited to, compliance with advertising and promotion regulations enforced by FDA's Office of Prescription Drug Promotion, the Prescription Drug Marketing Act, anti-fraud and abuse laws, healthcare information privacy laws, post-marketing safety surveillance, and disclosure of payments or transfers of value to healthcare professionals. In addition, we are subject to other federal and state regulation including, but not limited to, implementation of corporate compliance programs and reporting of payments and transfers of value to healthcare professionals.

Outside of the United States, our ability to market a product is contingent 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. At present,

foreign marketing authorizations are applied for at a national level, although within the European Community, or EC, registration procedures are available to companies wishing to market a product in more than one EC member state. If the regulatory authority is satisfied that adequate evidence of safety, quality and efficacy has been presented, marketing authorization will be granted. This foreign regulatory approval process involves all of the risks associated with FDA marketing approval discussed above. In addition, foreign regulations may include applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

#### **Drugs for Serious or Life-Threatening Illnesses**

The Federal Food, Drug and Cosmetic Act, as amended, and FDA regulations provide certain mechanisms for the accelerated "Fast Track" approval of potential products intended to treat serious or life-threatening illnesses which have been studied for safety and effectiveness and which demonstrate the potential to address unmet medical needs. These procedures permit early consultation and commitment from the FDA regarding the preclinical and clinical studies necessary to gain marketing approval. Provisions of this regulatory framework also permit, in certain cases, NDAs to be approved on the basis of valid surrogate markers of product effectiveness, thus accelerating the normal approval process. Certain potential products employing our technology might qualify for this accelerated regulatory procedure. Even if the FDA agrees that these potential products qualify for accelerated approval procedures, the FDA may deny approval of our drugs or may require that additional studies be required before approval. The FDA may also require us to perform post-approval, or Phase IV, studies as a condition of such early approval. In addition, the FDA may impose restrictions on distribution and/or promotion in connection with any accelerated approval, and may withdraw approval if post-approval studies do not confirm the intended clinical benefit or safety of the potential product.

#### **Coverage and Reimbursement**

Market acceptance and sales of any product candidates for which we may receive regulatory approval will depend, in part, upon the availability of coverage and adequate reimbursement to healthcare providers from third-party payors. Third-party payors such as government health programs (including Medicare and Medicaid in the United States), managed care organizations, private health insurers, and other organizations generally decide which drugs they will pay for and establish reimbursement levels for health care. Coverage decisions may depend upon various clinical and economic factors that potentially disfavor new drug products when more established or lower cost therapeutic alternatives are available. Even if coverage is made available by a third-party payor, the reimbursement rates paid for covered products might not be adequate. The marketability of any products for which we may receive regulatory approval for commercial sale may suffer if the government and other third-party payors fail to provide coverage and adequate reimbursement to allow us to sell such products on a competitive and profitable basis. For example, under these circumstances, physicians may limit how much or under what circumstances they will prescribe or administer such products, and patients may decline to purchase them. This, in turn, could affect our ability to successfully commercialize our products and impact our profitability, results of operations, financial condition, and future success.

In the United States and other potentially significant markets for our product candidates, government authorities and third party payors are increasingly attempting to limit or regulate the price of medical products and services, particularly for new and innovative products and therapies. Such pressure, along with the increased emphasis on managed healthcare in the United States and on country and regional pricing and reimbursement controls in other countries, will likely put additional downward pressure on product pricing, reimbursement and usage, which may adversely affect any future product sales and our results of operations. The market for any product candidates for which we may receive regulatory approval will depend significantly on the degree to which these products are listed on third-party payors' drug formularies, or lists of medications for which third-party payors provide coverage and reimbursement, to the extent products for which we may receive regulatory approval are covered under a pharmacy benefit or are otherwise subject to a formulary. The industry

competition to be included on such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payors may refuse to include a particular branded drug on their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other therapeutic alternative is available. In addition, because each third-party payor individually approves coverage and reimbursement levels, obtaining coverage and adequate reimbursement is a time-consuming and costly process. We may be required to provide scientific and clinical support for the use of any product to each third-party payor separately with no assurance that approval would be obtained, and we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. We cannot be certain that our product candidates will be considered cost-effective. This process could delay the market acceptance of any product candidates for which we may receive approval and could have a negative effect on our future revenues and operating results.

In the United States, the Medicare Part D program provides a voluntary outpatient drug benefit to Medicare beneficiaries for certain products. We expect pimavanserin, if approved, will be available for coverage under Medicare Part D, but the extent to which the individual Part D plans may offer coverage may be subject to various factors such as those described above. In addition, while Medicare Part D has historically required Medicare Part D plans to include "all or substantially all" drugs in the following designated classes of "clinical concern" on their formularies: anticonvulsants, antidepressants, antineoplastics, antipsychotics, antiretrovirals, and immunosuppressants, the government has recently proposed changing this policy. Importantly, the government has proposed that, for coverage year 2015, the "all or substantially all" policy be limited to anticonvulsants, antiretrovirals, and antineoplastics, and that "the antipsychotic drug class continue to be treated as a class of "clinical concern" in 2015 unless and until the Centers for Medicare & Medicaid Services, or CMS, determines otherwise. This policy has not been finalized at this time, however, if the policy was adopted and if CMS stopped "protecting" the antipsychotic class, Medicare Part D plans would have significantly more discretion to reduce the number of products covered in that class. Furthermore, private payors often follow Medicare coverage policies and payment limitations in setting their own coverage policies.

Coverage policies, third-party reimbursement rates, and product pricing regulation may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products that receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

#### "Fraud and Abuse", Data Privacy, and Security Laws and Regulations

In addition to FDA restrictions on marketing of pharmaceutical products, federal and state fraud and abuse laws restrict business practices in the pharmaceutical industry. These laws include anti-kickback and false claims laws and regulations as well as data privacy and security laws and regulations. The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting, or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value, and thus the Anti-Kickback Statute could potentially restrict certain arrangements between pharmaceutical manufacturers and customers that are common, innocuous, or even potentially beneficial in other industries. Although there are a number of statutory exemptions and regulatory safe harbors protecting some common activities from prosecution, the exemptions and safe harbors are limited in scope. The Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, among other things, amended the intent requirement of the federal Anti-Kickback Statute to state that a person or entity need not have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Where "one purpose" of an arrangement involving remuneration is to induce referrals of a federal healthcare covered business, the statute may have been violated, and enforcement will depend on the relevant facts and circumstances.

The federal False Claims Act prohibits any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, using or causing to be made or used a

false record or statement material to a false or fraudulent claim to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. In addition, the ACA specified that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act. The federal False Claims Act has been the basis for numerous enforcement actions and settlements by pharmaceutical and other healthcare companies in connection with various alleged financial relationships with customers. In addition, a number of pharmaceutical companies have reached substantial financial settlements in connection with allegedly causing false claims to be submitted because of their marketing of products for unapproved, and thus non-reimbursable, uses.

Separately, there are a number of other fraud and abuse laws to which pharmaceutical companies are subject, particularly after a product candidate has been approved for marketing in the United States. For example, a federal criminal law enacted as part of the Health Insurance Portability and Accountability Act of 1996, or HIPAA, prohibits knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third party payors, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Also, many states have similar fraud and abuse statutes or regulations, including, without limitation, laws analogous to the federal Anti-Kickback Statute and the federal False Claims Act, that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and their respective implementing regulations, impose specified requirements relating to the privacy, security, and transmission of certain individually identifiable health information. Among other things, HIPAA's privacy and security standards are now directly applicable to "business associates", which is defined as independent contractors or agents of covered entities that create, receive, maintain, or transmit protected health information in connection with providing a service for or on behalf of a covered entity. In addition to possible civil and criminal penalties for violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, which further complicates compliance efforts.

There are also an increasing number of state "sunshine" laws that require pharmaceutical companies to make reports to states on pricing and marketing information. Several states have enacted legislation requiring pharmaceutical companies to, among other things, establish marketing compliance programs, file periodic reports with the state, and make periodic public disclosures on sales and marketing activities, and prohibiting certain other sales and marketing practices. In addition, a federal requirement mandates that pharmaceutical companies track and report to the federal government certain payments and other transfers of value made to physicians and other healthcare professionals and teaching hospitals and ownership or investment interests held by physicians and their immediate family members. The federal government will disclose the reported information on a publicly available website beginning in 2014. These laws may adversely affect our sales, marketing, and other activities with respect to any product candidate for which we receive approval to market in the United States by imposing administrative and compliance burdens on us. If we fail to track and report as required by these laws or otherwise fail to comply with these laws, we could be subject to the penalty provisions of the pertinent state and federal authorities.

Because of the breadth of these laws and the narrowness of available statutory and regulatory exemptions, it is possible that some of our business activities, particularly any sales and marketing activities after a product candidate has been approved for marketing in the United States, could be subject to legal challenge and enforcement actions. If our operations are found to be in violation of any of the federal and state laws described above or any other governmental regulations that apply to us, we may be subject to significant civil, criminal,

and administrative penalties, including, without limitation, damages, fines, imprisonment, exclusion from participation in government healthcare programs, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our product candidates receive approval and are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs, as well as laws and regulations requiring transparency of pricing and marketing information and governing the privacy and security of health information, such as the European Union's Directive 95/46/EC on the protection of individuals with regard to the processing of personal data.

#### Impact of Healthcare Reform on Coverage, Reimbursement, and Pricing

In the United States, the European Union and other potentially significant markets for our product candidates, government authorities and third-party payers are increasingly attempting to limit or regulate the price of medical products and services, particularly for new and innovative products and therapies, which has resulted in lower average selling prices. Further, the increased emphasis on managed healthcare in the United States and on country-specific and regional pricing and reimbursement controls in the European Union will put additional pressure on product pricing, reimbursement and usage, which may adversely affect our future product sales and results of operations. These pressures can arise from rules and practices of managed care groups, judicial decisions, and governmental laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical reimbursement policies, and pricing in general.

The United States and some foreign jurisdictions are considering or have enacted a number of additional legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell any future products profitably. Among policy makers and payers in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives, including, most recently, the ACA. The ACA, among other things, imposes a significant annual fee on companies that manufacture or import branded prescription drug products. It also contains substantial new provisions intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, and impose additional health policy reforms, any or all of which may affect our business. A significant number of provisions are not yet, or have only recently become, effective, but the ACA is likely to continue the downward pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs. Other legislative changes have also been proposed and adopted since the ACA was enacted. For example, the Budget Control Act of 2011 resulted in aggregate reductions in Medicare payments to providers of up to 2% per fiscal year, starting in 2013, and the American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Such laws may result in additional reductions in Medicare and other healthcare funding. In the future, there may continue to be additional proposals relating to the reform of the U.S. healthcare system, some of which could further limit coverage and reimbursement of drug products, including our product candidates. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

#### Marketing, Sales and Distribution

We are establishing a small commercial organization that is designed to help prepare for the planned future launch of our lead product candidate, pimavanserin. This includes experienced professionals in marketing, reimbursement and managed markets, marketing research, commercial operations, and sales force planning and management. We have not yet established field sales or distribution capabilities. In order to commercialize any of

our product candidates, including pimavanserin, we must develop these capabilities internally or through collaboration with third parties. In selected therapeutic areas where we feel that our product candidates can be commercialized by a specialty sales force that calls on a limited and focused group of physicians, we plan to commercialize our product candidates in the United States. In therapeutic areas that require a large sales force selling to a large and diverse prescribing population, we may elect to commercialize through, or in collaboration with, strategic partners. We may choose to commercialize our products in selected markets outside of the United States by establishing one or more strategic alliances.

#### **Manufacturing**

We outsource and plan to continue to outsource manufacturing responsibilities for our existing and future product candidates, including pimavanserin, for development and commercial purposes. The production of pimavanserin employs small molecule synthetic organic chemistry procedures that are standard in the pharmaceutical industry. Our collaboration agreements provide for our partners to arrange for the production of our product candidates for use in clinical trials and potential commercialization.

#### **Employees**

At December 31, 2013, we had 48 employees, of whom 23 hold Ph.D. or other advanced degrees. Of our total workforce, 29 are engaged in research and development activities and 19 are engaged in executive, finance, commercial, and administration activities. None of our employees is represented by a collective bargaining agreement, nor have we experienced work stoppages. We believe that our relations with our employees are good.

#### **Research and Development Expenses**

Our research and development expenses were \$26.7 million in 2013, \$18.8 million in 2012, and \$17.3 million in 2011.

#### **Long-Lived Assets**

Our long-lived assets totaled \$579,000 and \$42,000 as of December 31, 2013 and 2012, respectively. All of our long-lived assets are located in the United States.

#### Item 1A. Risk Factors.

You should consider carefully the following information about the risks described below, together with the other information contained in this Annual Report and in our other public filings in evaluating our business. If any of the following risks actually occurs, our business, financial condition, results of operations and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock would likely decline.

#### **Risks Related to Our Business**

Our prospects are highly dependent on the success of pimavanserin, our most advanced product candidate. To the extent regulatory approval of pimavanserin is delayed or not granted or pimavanserin is not commercially successful, our business, financial condition and results of operations may be materially adversely affected and the price of our common stock may decline.

We currently have no product candidates approved for sale, and we may never be able to develop marketable products. The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of pharmaceutical product candidates are subject to extensive regulation by the U.S. Food and Drug Administration, or FDA, and other regulatory authorities in the United States and other countries, whose regulations differ from country to country. We are focusing a significant portion of our activities and resources on pimavanserin, and we believe our prospects are highly dependent on, and a significant portion of the value of our company relates to,

our ability to obtain regulatory approval for and successfully commercialize pimavanserin in the United States and potentially in additional territories. The regulatory approval and successful commercialization of pimavanserin is subject to many risks, including the risks discussed in other risk factors, and pimavanserin may not receive marketing approval from any regulatory agency. If the results or timing of regulatory filings, the regulatory process, regulatory developments, commercialization, clinical trials or preclinical studies, or other activities, actions or decisions related to pimavanserin do not meet our or others' expectations, the market price of our common stock could decline significantly.

In April 2013, we announced that the FDA had agreed that the data from our -020 study, together with supportive data from our other studies with pimavanserin, are sufficient to support the filing of a New Drug Application, or NDA, for the treatment of Parkinson's disease psychosis, or PDP. We are currently focused on completing the remaining elements of our pimavanserin Parkinson's disease psychosis development program that are needed for submission of an NDA. These include customary supportive studies, such as drug-drug interaction studies, and Chemistry, Manufacturing and Controls, or CMC, development, such as stability testing of registration batches. While the FDA has agreed to accept and review an NDA for pimavanserin on the basis of our positive pivotal -020 study data, along with supportive efficacy and safety data from other pimavanserin studies, the NDA will be subject to a standard FDA review to determine whether the entire filing package is adequate to support approval of pimavanserin for PDP. We plan to have pre-NDA meetings with the FDA and may learn that additional studies or CMC development that we are not currently expecting are required before the pimavanserin NDA would be accepted for filing by the FDA. Notwithstanding the guidance that we received in April 2013, the FDA retains complete discretion in deciding whether to file an NDA for pimavanserin and there are many components to an NDA submission beyond the efficacy and safety data reviewed by the FDA in 2013. Even if our NDA submission for pimavanserin is accepted for filing, the FDA retains complete discretion in deciding whether or not to approve an NDA and there is no guarantee that pimavanserin will be approved for the treatment of PDP. Thus, significant uncertainty remains regarding the clinical development and regulatory approval process for pimavanserin.

## Even if the FDA grants us approval of pimavanserin for PDP, the terms of the approval may limit its commercial potential.

The FDA has complete discretion over the approval of pimavanserin for PDP. If it grants approval, the scope of the approval may limit our ability to commercialize pimavanserin, and in turn, limit our ability to generate substantial sales revenues. For example, the FDA may not approve the labeling claims for pimavanserin that we believe are necessary or desirable for successful commercialization as a treatment for PDP, or may grant approval contingent on the performance of costly post-approval clinical trials or subject to warnings or contraindications. Additionally, even after granting approval, the FDA may decide to withdraw approval, add warnings or narrow the approved indications in the product label, or establish risk management programs that could restrict distribution. These actions could result from, among other things, safety concerns, including unexpected side effects or drug-drug interaction problems, or concerns over misuse or abuse of the product. If any of these actions were to occur following approval, we may have to discontinue the commercialization of pimavanserin, limit our sales and marketing efforts, and/or conduct post-approval studies, which in turn could result in significant expense and delay or limit our ability to generate sales revenues.

## If we do not obtain regulatory approval from foreign jurisdictions, we will not be able to market our products in those jurisdictions which will limit our commercial revenues.

In order to market our products in foreign jurisdictions, we must obtain foreign regulatory approval in each of those jurisdictions. Approval by the FDA does not ensure that foreign jurisdictions will also approve our products for commercial distribution. The regulations in foreign jurisdictions vary, we will be required to comply with different regulations and policies of the jurisdictions where we seek approval for our product candidates, and we have not yet identified all of the requirements that will be required by us to submit pimavanserin for approval in foreign jurisdictions. This will require additional time, expertise and expense, including the potential

need to conduct additional studies or development work beyond that required to obtain regulatory approval in the United States. Furthermore, we may not be able to obtain approval for foreign sales. This will restrict our ability to market our products and would limit their commercial potential and value.

### We expect our net losses to continue for at least several years and are unable to predict the extent of future losses or when we will become profitable, if ever.

We have experienced significant net losses since our inception. As of December 31, 2013, we had an accumulated deficit of approximately \$405.7 million. We expect to incur net losses over the next several years as we advance our programs and incur significant development and commercialization costs.

We have not received any revenues from the commercialization of our product candidates. We plan to submit our NDA for pimavanserin in PDP near the end of 2014. The regulatory approval process is time consuming and uncertain and there is no guarantee that our planned NDA submission for pimavanserin will be accepted for filing or, if accepted, approved for marketing. Even if our NDA for pimavanserin is approved, we would still expect to incur significant expenses and net losses for at least several years as we begin our first ever commercialization efforts and pursue the development and commercialization of pimavanserin and other product candidates. Substantially all of our revenues for the year ended December 31, 2013 were from our collaborations with Allergan and our agreements with other parties, including our research and development grants. The research term of our 2003 collaboration with Allergan concluded in March 2013 and we no longer recognize revenues from this collaboration. Thus, any additional payments from Allergan pursuant to our continuing collaborations are dependent upon the advancement of our applicable product candidates. Until such time as we may gain regulatory approval for, and generate revenues from, product sales, we anticipate that collaborations, which provide us with research funding and potential milestone payments and royalties, and grant funding will continue to be our primary sources of revenues.

We cannot be certain that the milestones required to trigger payments under our existing collaborations will be reached or that we will secure additional collaboration agreements. To obtain revenues from our product candidates, we must succeed, either alone or with others, in developing, obtaining regulatory approval for, manufacturing and marketing drugs with significant market potential. We may never succeed in these activities and may never generate revenues that are significant enough to achieve profitability.

# The pivotal Phase III study with pimavanserin for PDP, the results of which were announced in November 2012, was our first successful pivotal Phase III trial and there is no guarantee that future studies with pimavanserin will be successful.

The historical rate of failures for product candidates in clinical development is extremely high. In November 2012, we announced results from our successful pivotal -020 Phase III trial with pimavanserin for the treatment of PDP. Following our April 2013 meeting with the FDA, we have been conducting customary supportive studies, such as drug-drug interaction studies and CMC development, which are needed prior to filing an NDA. Even though we successfully completed the -020 study, those results are not predictive of results of the supportive studies and CMC development needed before an NDA may be submitted to the FDA. We believe that pimavanserin also may have utility in indications other than PDP, such as Alzheimer's disease psychosis, or ADP, and schizophrenia. However, prior to the first efficacy study that we commenced in late 2013, we have never tested pimavanserin in clinical studies for ADP and we have only conducted a Phase II trial for pimavanserin as a co-therapy treatment in schizophrenia. There is no guarantee that we will have the same level of success with pimavanserin in other indications that we had with the -020 study or that we will be successful at all in future studies for additional indications.

If we do not successfully complete development of pimavanserin, we will be unable to market and sell products derived from it and to generate related product revenues. Of the large number of drugs in development, only a small percentage result in the submission of an NDA to the FDA and even fewer are approved for commercialization.

### We depend on collaborations with third parties to develop and commercialize selected product candidates and to provide substantially all of our revenues.

One aspect of our strategy is to selectively enter into collaboration agreements with third parties. We currently rely, and will continue to rely, on our collaborators for financial resources and for development, regulatory, and commercialization expertise for selected product candidates. Our 2003 research agreement with Allergan ended in March 2013, and additional payments from our two ongoing agreements with Allergan are dependent upon successful advancement of our applicable product candidates. Unless these milestones are met, we will not receive future revenues from our current collaborations with Allergan.

Our collaborators may fail to develop or effectively commercialize products using our product candidates or technologies because they:

- do not have sufficient resources or decide not to devote the necessary resources due to internal constraints such as limited cash or human resources or a change in strategic focus;
- decide to pursue a competitive product developed outside of the collaboration; or
- cannot obtain the necessary regulatory approvals.

For example, Allergan has announced that it is seeking a partner for further development and commercialization of drug candidates in our chronic pain program. If Allergan is unable to successfully partner this program, it may elect to not pursue further development. In addition, any partner that Allergan does identify may devote substantially less resources than Allergan has devoted to our chronic pain program to date.

In addition, Allergan can terminate our existing collaborations upon prior notice to us. We may not be able to renew our other existing collaborations on acceptable terms, if at all. We also face competition in our search for new collaborators, if we seek a new partner for our pimavanserin program or other programs. Given the current economic environment, it is possible that competition for new collaborators may increase. If we are unable to renew any existing collaboration or find new collaborations, we may not be able to continue advancing our programs alone.

## If we fail to obtain the capital necessary to fund our operations, we will be unable to successfully develop products.

We have consumed substantial amounts of capital since our inception. Our cash, cash equivalents and investment securities totaled \$185.8 million at December 31, 2013. While we believe that our existing cash resources will be sufficient to fund our cash requirements at least through 2015, we will require significant additional financing in the future to continue to fund our operations. Our future capital requirements will depend on, and could increase significantly as a result of, many factors including:

- the progress in, and the costs of, our development and pre-commercialization activities for pimavanserin and other research and development programs;
- the costs of preparing applications for regulatory approvals for our product candidates and the timing of any approvals;
- the costs of establishing, or contracting for, sales and marketing capabilities;
- the scope, prioritization and number of our research and development programs;
- the ability of our collaborators and us to reach the milestones and other events or developments triggering payments under our collaboration or license agreements, or our collaborators ability to make payments under these agreements;
- our ability to enter into new, and to maintain existing, collaboration and license agreements;
- the extent to which we are obligated to reimburse collaborators or collaborators are obligated to reimburse us for costs under collaboration agreements;

- the costs involved in filing, prosecuting, enforcing and defending patent claims and other intellectual property rights;
- the costs of securing manufacturing arrangements for clinical or commercial production of product candidates; and
- the costs associated with litigation.

Until we can generate significant continuing revenues, we expect to satisfy our future cash needs through our existing cash, cash equivalents and investment securities, strategic collaborations, public or private sales of our securities, debt financings, grant funding, or by licensing all or a portion of our product candidates or technology. In the past, periods of turmoil and volatility in the financial markets have adversely affected the market capitalizations of many biotechnology companies, and generally made equity and debt financing more difficult to obtain. These events, coupled with other factors, may limit our access to additional financing in the future. This could have a material adverse effect on our ability to access sufficient funding. We cannot be certain that additional funding will be available to us on acceptable terms, if at all. If funds are not available, we will be required to delay, reduce the scope of, or eliminate one or more of our research or development programs or our commercialization efforts. We also may be required to relinquish greater or all rights to product candidates at an earlier stage of development or on less favorable terms than we would otherwise choose. Additional funding, if obtained, may significantly dilute existing stockholders and could negatively impact the price of our stock.

# We do not have a partner for the development of our lead product candidate, pimavanserin, and are solely responsible for the advancement of this program and, if approved for marketing, commercialization of the product.

We have full responsibility for the pimavanserin program throughout the world. We expect our research and development costs for continued development of pimavanserin to be substantial. While we currently are undertaking the ongoing development work for pimavanserin, including supportive studies and CMC work for an NDA filing, in the future we would need to add resources and raise additional funds in order to take this product candidate to market and to conduct the necessary sales and marketing activities, if we do not secure a partner. Following any potential approval by the FDA, our current strategy is to commercialize pimavanserin for Parkinson's disease psychosis in the United States by establishing a specialty sales force focused primarily on neurologists. In addition, if we commercialize pimavanserin in select markets outside of the United States, we will more than likely need to establish one or more strategic alliances in the future for that purpose. Without future collaboration partners in the United States and abroad, we might not be able to realize the full value of pimavanserin.

#### Even if pimavanserin is approved by the FDA for PDP, we may not be successful in its commercial launch.

We currently have a small commercialization group but have never, as an organization, launched or commercialized a product. Following any potential approval by the FDA, in addition to building a sales force, we will need to successfully coordinate the commercialization of the product. Prior to commercialization, pimavanserin could also be subject to review and potential scheduling by the Drug Enforcement Administration of the US Department of Justice, or DEA, which could adversely impact its marketing and commercialization. There are numerous examples of unsuccessful product launches and, since we have never launched a product, there is no guarantee that we will be able to do so if granted marketing approval for pimavanserin for PDP. If any product launch of pimavanserin is unsuccessful or perceived as disappointing, our stock price could decline significantly and the long-term success of the product could be harmed.

## Our most advanced product candidates are in development, which is a long, expensive and unpredictable process, and there is a high risk of failure.

Preclinical testing and clinical trials are long, expensive and unpredictable processes that can be subject to delays. It may take several years to complete the preclinical testing and clinical development necessary to commercialize a drug, and delays or failure can occur at any stage. Interim results of clinical trials do not

necessarily predict final results, and success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials even after promising results in earlier trials.

Our drug development programs are at various stages of development and the historical rate of failures for product candidates is extremely high. In fact, we ended Phase I testing of AM-831 in 2012 and had previously had an unsuccessful Phase III trial with our most advanced product candidate, pimavanserin. Following the reporting of successful results from the Phase III -020 study with pimavanserin in November 2012 and our meeting with the FDA in April 2013, we are conducting customary supportive studies, such as drug-drug interaction studies, and CMC development, such as stability testing of registration batches, prior to our planned submission of an NDA for pimavanserin in PDP near the end of 2014. An unfavorable outcome in any of the foregoing development efforts for pimavanserin would be a major set-back for the program and for us, generally. In particular, an unfavorable outcome in our pimavanserin program may require us to delay, reduce the scope of, or eliminate this program and could have a material adverse effect on us and the value of our common stock. In addition to our PDP program with pimavanserin, we commenced a Phase II study with pimavanserin for patients with ADP in November 2013 and we are planning additional studies in other indications, including schizophrenia. We also have clinical programs in collaboration with Allergan for the treatment of chronic pain and glaucoma, which have reached Phase II and Phase I development, respectively.

In connection with clinical trials, we face risks that:

- a product candidate may not prove to be efficacious;
- patients may die or suffer other adverse effects for reasons that may or may not be related to the product candidate being tested;
- the results may not be consistent with positive results of earlier trials; and
- the results may not meet the level of statistical significance required by the FDA or other regulatory agencies.

If we do not successfully complete preclinical and clinical development, we will be unable to market and sell products derived from our product candidates and to generate product revenues. Even if we do successfully complete clinical trials, those results are not necessarily predictive of results of additional trials that may be needed before an NDA may be submitted to the FDA. Of the large number of drugs in development, only a small percentage result in the submission of an NDA to the FDA and even fewer are approved for commercialization.

# Delays, suspensions and terminations in our clinical trials could result in increased costs to us and delay our ability to generate product revenues.

The commencement of clinical trials can be delayed for a variety of reasons, including delays in:

- demonstrating sufficient safety and efficacy to obtain regulatory approval to commence a clinical trial;
- reaching agreement on acceptable terms with prospective contract research organizations and clinical trial sites;
- manufacturing sufficient quantities of a product candidate;
- obtaining clearance from the FDA to commence clinical trials pursuant to an Investigational New Drug application;
- obtaining institutional review board approval to conduct a clinical trial at a prospective clinical trial site;
- patient enrollment, which is a function of many factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical trial sites, the availability of effective treatments for the relevant disease and the eligibility criteria for the clinical trial.

Once a clinical trial has begun, it may be delayed, suspended or terminated due to a number of factors, including:

- ongoing discussions with regulatory authorities regarding the scope or design of our clinical trials or requests by them for supplemental information with respect to our clinical trial results;
- failure to conduct clinical trials in accordance with regulatory requirements;
- lower than anticipated screening or retention rates of patients in clinical trials;
- serious adverse events or side effects experienced by participants; and
- insufficient supply or deficient quality of product candidates or other materials necessary for the conduct of our clinical trials.

Many of these factors may also ultimately lead to denial of regulatory approval of a current or potential product candidate. If we experience delays, suspensions or terminations in a clinical trial, the commercial prospects for the related product candidate will be harmed, and our ability to generate product revenues will be delayed.

### If conflicts arise with our collaborators, they may act in their self-interests, which may be adverse to our interests.

Conflicts may arise in our collaborations due to one or more of the following:

- disputes or breaches with respect to payments that we believe are due under the applicable agreements, particularly in the current economic environment when companies, including large established ones, may be seeking to reduce external payments;
- disputes on strategy as to what development or commercialization activities should be pursued under the applicable agreements;
- disputes as to the responsibility for conducting development and commercialization activities pursuant to the applicable collaboration, including the payment of costs related thereto;
- disagreements with respect to ownership of intellectual property rights;
- unwillingness on the part of a collaborator to keep us informed regarding the progress of its development and commercialization activities, or to permit public disclosure of these activities;
- delay of a collaborator's development or commercialization efforts with respect to our product candidates; or
- termination or non-renewal of the collaboration.

Conflicts arising with our collaborators could impair the progress of our product candidates, harm our reputation, result in a loss of revenues, reduce our cash position, and cause a decline in our stock price.

In addition, in our collaborations, we generally have agreed not to conduct independently, or with any third party, any research that is directly competitive with the research conducted under the applicable program. Our collaborations may have the effect of limiting the areas of research that we may pursue, either alone or with others. Our collaborators, however, may develop, either alone or with others, products in related fields that are competitive with the products or potential products that are the subject of these collaborations. Competing products, either developed by our collaborators or to which our collaborators have rights, may result in the allocation of resources by our collaborators to competing products and their withdrawal of support for our product candidates or may otherwise result in lower demand for our potential products.

We have collaborations with Allergan for the development of product candidates related to chronic pain and ophthalmic diseases, including glaucoma. Allergan currently markets therapeutic products to treat glaucoma and

is engaged in other research programs related to glaucoma and other ophthalmic products that are independent from our development program in this therapeutic area. Allergan is also pursuing other research programs related to pain management that are independent from our collaboration in this therapeutic area.

# We rely on third parties to conduct our clinical trials and perform data collection and analysis, which may result in costs and delays that prevent us from successfully commercializing product candidates.

Although we design and manage our current preclinical studies and clinical trials, we currently do not have the ability to conduct clinical trials for our product candidates on our own. In addition to our collaborators, we rely on contract research organizations, medical institutions, clinical investigators, and contract laboratories to perform data collection and analysis and other aspects of our clinical trials. In addition, we also rely on third parties to assist with our preclinical studies, including studies regarding biological activity, safety, absorption, metabolism, and excretion of product candidates.

Our preclinical activities or clinical trials may be delayed, suspended, or terminated if:

- these third parties do not successfully carry out their contractual duties or fail to meet regulatory obligations or expected deadlines;
- these third parties need to be replaced; or
- the quality or accuracy of the data obtained by these third parties is compromised due to their failure to adhere to our clinical protocols or regulatory requirements or for other reasons.

Failure to perform by these third parties may increase our development costs, delay our ability to obtain regulatory approval, and delay or prevent the commercialization of our product candidates. We currently use several contract research organizations to perform services for our preclinical studies and clinical trials. While we believe that there are numerous alternative sources to provide these services, in the event that we seek such alternative sources, we may not be able to enter into replacement arrangements without delays or additional expenditures.

# Even if we or our collaborators successfully complete the clinical trials of product candidates, the product candidates may fail for other reasons.

Even if we or our collaborators successfully complete the clinical trials of product candidates, the product candidates, such as pimavanserin, may fail for other reasons, including the possibility that the product candidates will:

- fail to receive the regulatory clearances required to market them as drugs;
- be subject to proprietary rights held by others requiring the negotiation of a license agreement prior to marketing;
- be difficult or expensive to manufacture on a commercial scale;
- have adverse side effects that make their use less desirable; or
- fail to compete with product candidates or other treatments commercialized by competitors.

# Relying on third-party manufacturers may result in delays in our clinical trials, regulatory approvals and product introductions.

We have no manufacturing facilities and only limited experience in the manufacturing of drugs or in designing drug-manufacturing processes. We have contracted with third-party manufacturers to produce, in collaboration with us, our product candidates, including pimavanserin, for clinical trials. If any of our product candidates are approved by the FDA or other regulatory agencies for commercial sale, we will need to contract with a third party to manufacture them in larger quantities. While we believe that there will be alternative sources

available to manufacture our product candidates, including pimavanserin, in the event that we seek such alternative sources, we may not be able to enter into replacement arrangements without delays or additional expenditures. We cannot estimate these delays or costs with certainty but, if they were to occur, they could cause a delay in our development and commercialization efforts. We have not yet entered into long-term agreements with our current third-party manufacturers or with any alternate suppliers. Although we intend to do so prior to any commercial launch of a product that is approved by the FDA in order to ensure that we maintain adequate supplies of commercial drug product, we may be unable to enter into such agreements or do so on commercially reasonable terms, which could delay a product launch or subject our commercialization efforts to significant supply risk.

The manufacturers of our product candidates are obliged to operate in accordance with FDA-mandated current good manufacturing practices, or cGMPs. In addition, the facilities used by our contract manufacturers or other third party manufacturers to manufacture our product candidates must be approved by the FDA pursuant to inspections that will be conducted after we request regulatory approval from the FDA. A failure by any of our contract manufacturers to establish and follow cGMPs or to document their adherence to such practices may lead to significant delays in clinical trials or in obtaining regulatory approval of product candidates or the ultimate launch of products based on our product candidates into the market. Failure by our third-party manufacturers or us to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, failure of the government to grant pre-market approval of drugs, delays, suspension or withdrawal of approvals, seizures or recalls of products, operating restrictions, and criminal prosecutions.

# Our product candidates, including pimavanserin, may not gain acceptance among physicians, patients, and the medical community, thereby limiting our potential to generate revenues.

Even if our product candidates are approved for commercial sale by the FDA or other regulatory authorities, the degree of market acceptance of any approved product candidate by physicians, healthcare professionals and third-party payors, and our profitability and growth will depend on a number of factors, including:

- the ability to provide acceptable evidence of safety and efficacy;
- relative convenience and ease of administration;
- the prevalence and severity of any adverse side effects;
- availability of alternative treatments;
- pricing and cost effectiveness, which may be subject to regulatory control;
- effectiveness of our or our collaborators' sales and marketing strategy; and
- our ability to obtain sufficient third-party insurance coverage or adequate reimbursement levels.

If any product candidate that we discover and/or develop does not provide a treatment regimen that is as beneficial as the current standard of care or otherwise does not provide patient benefit, that product will not achieve market acceptance and we will not generate sufficient revenues to achieve or maintain profitability.

If we are unable to attract, retain, and motivate key management and research and development staff, our drug development programs and our research and discovery efforts may be delayed and we may be unable to successfully develop or commercialize our product candidates, including pimavanserin.

Our success depends on our ability to attract, retain, and motivate highly qualified management and scientific personnel. In particular, our development programs depend on our ability to attract and retain highly skilled development personnel, especially in the fields of central nervous system disorders, including neuropsychiatric and related disorders. In the future, we expect to need to hire additional personnel as we expand our research and development efforts and commercial activities for pimavanserin from our current levels. We face competition for experienced scientists, clinical operations personnel, commercial and other personnel from

numerous companies and academic and other research institutions. Competition for qualified personnel is particularly intense in the San Diego, California area. In addition, our Chief Financial Officer, who has been with the Company since 1998 and also serves as our Chief Business Officer, announced in January 2014 that he would be retiring. While we have begun to recruit a replacement, there is no guarantee that we will be able to replace the skills and expertise of our retiring Chief Financial Officer and we may experience difficulties in transitioning this position, which could adversely impact us. If we are unable to attract and retain the necessary personnel for this and other positions, this will significantly impede the achievement of our research and development objectives, our commercialization efforts for pimavanserin, and our ability to meet the demands of our collaborators in a timely fashion.

All of our employees are "at will" employees, which means that any employee may quit at any time and we may terminate any employee at any time. We do not carry "key person" insurance covering members of senior management.

### We do not know whether our drug discovery platform will lead to the discovery or development of commercially viable product candidates.

Our drug discovery platform uses unproven methods to identify and develop product candidates, including pimavanserin. We have never successfully completed clinical development of any of our product candidates, and there are no drugs on the market that have been discovered using our drug discovery platform.

Our research and development focuses on small molecule drugs for the treatment of central nervous system disorders. Due to our limited resources, we may have to forego potential opportunities with respect to discovering product candidates to treat diseases or conditions in other therapeutic areas. If we are not able to use our technologies to discover and develop product candidates that can be commercialized, we may not achieve profitability. In the future, we will likely find it necessary to license the technology of others or acquire additional product candidates to augment the results of our internal discovery activities. If we are unable to identify new product candidates using our drug discovery platform, we may be unable to establish or maintain a clinical development pipeline or generate product revenues.

# We may not be able to continue or fully exploit our collaborations with outside scientific and clinical advisors, which could impair the progress of our clinical trials and our research and development efforts.

We work with scientific and clinical advisors at academic and other institutions who are experts in the field of central nervous system disorders. They assist us in our research and development efforts and advise us with respect to our clinical trials. These advisors are not our employees and may have other commitments that would limit their future availability to us. Although our scientific and clinical advisors generally agree not to engage in competing work, if a conflict of interest arises between their work for us and their work for another entity, we may lose their services, which may impair our reputation in the industry and delay the development or commercialization of our product candidates.

# We will need to continue to manage our organization and we may encounter difficulties with our staffing and any future growth, which could adversely affect our results of operations.

We will need to effectively manage our operations and facilities in order to advance our drug development programs, including those covered by our collaborations with Allergan, achieve milestones under our collaboration agreements, facilitate additional collaborations, and pursue other development and commercialization activities. As we advance the pimavanserin program towards submitting an NDA, we already have added several capabilities. However, we will need to add qualified personnel and resources if the NDA is approved for marketing and we establish a commercial sales force. Our current infrastructure will be inadequate to support these future efforts and expected growth. In particular, we will have to develop internal sales, marketing, and distribution capabilities if we decide to market any drug that we may successfully develop, including pimavanserin. We may not successfully manage our operations and, accordingly, may not achieve our research, development, and commercialization goals.

# We expect that our results of operations will fluctuate, which may make it difficult to predict our future performance from period to period.

Our operating results have fluctuated in the past and are likely to do so in future periods. Some of the factors that could cause our operating results to fluctuate from period to period include:

- the status of development and commercialization of pimavanserin and our other product candidates, including compounds being developed under our collaborations;
- whether we generate revenues or reimbursements by achieving specified research, development or commercialization milestones under any agreements or otherwise receive potential payments under these agreements;
- whether we are required to make payments due to achieving specified milestones under any licensing or similar agreements or otherwise make potential payments under these agreements;
- the incurrence of preclinical or clinical expenses that could fluctuate significantly from period to period, including reimbursement obligations pursuant to our collaboration agreements;
- the initiation, termination, or reduction in the scope of our collaborations or any disputes regarding these collaborations;
- the timing of our satisfaction of applicable regulatory requirements;
- the rate of expansion of our clinical development, other internal research and development efforts, and pre-commercial and commercial efforts;
- the effect of competing technologies and products and market developments;
- the costs associated with litigation; and
- general and industry-specific economic conditions.

We believe that comparisons from period to period of our financial results are not necessarily meaningful and should not be relied upon as indications of our future performance.

# Our management has broad discretion over the use of our cash and we may not use our cash effectively, which could adversely affect our results of operations.

Our management has significant flexibility in applying our cash resources and could use these resources for corporate purposes that do not increase our market value, or in ways with which our stockholders may not agree. We may use our cash resources for corporate purposes that do not yield a significant return or any return at all for our stockholders, which may cause our stock price to decline.

# We have incurred, and expect to continue to incur, significant costs as a result of laws and regulations relating to corporate governance and other matters.

Laws and regulations affecting public companies, including provisions of the Dodd-Frank Wall Street Reform and Consumer Protection Act that was enacted in July 2010, the provisions of the Sarbanes-Oxley Act of 2002, or SOX, and rules adopted or proposed by the SEC and by The NASDAQ Global Market, have resulted in, and will continue to result in, significant costs to us as we evaluate the implications of these rules and respond to their requirements. We issued an evaluation of our internal control over financial reporting under Section 404 of SOX with our Annual Report. In the future, if we are not able to issue an evaluation of our internal control over financial reporting as required or we or our independent registered public accounting firm determine that our internal control over financial reporting is not effective, this shortcoming could have an adverse effect on our business and financial results and the price of our common stock could be negatively affected. New rules could make it more difficult or more 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 coverage that is the same or similar to our current coverage. 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 and board committees, and as our executive officers. We cannot predict or estimate the total amount of the costs we may incur or the timing of such costs to comply with these rules and regulations.

### Our ability to generate product revenues will be diminished if our products do not receive coverage from payors or sell for inadequate prices, or if patients are unable to obtain adequate levels of reimbursement.

Patients who are prescribed medicine for the treatment of their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. Even if we obtain coverage for any approved products, the resulting reimbursement payment rates might not be adequate or may require co-payments that patients find unacceptably high. Patients are unlikely to use any products we may market unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of those products.

In addition, the market for any products for which we may receive regulatory approval will depend significantly on access to third-party payors' drug formularies, or lists of medications for which third-party payors provide coverage and reimbursement. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payors may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available.

Third-party payors, whether foreign or domestic, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In addition, in the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of any approved products to each payor separately, with no assurance that coverage will be obtained. If we are unable to obtain coverage of, and adequate payment levels for, our products from third-party payors, physicians may limit how much or under what circumstances they will prescribe or administer them and patients may decline to purchase them. This in turn could affect our ability to successfully commercialize any approved products and thereby adversely impact our profitability, results of operations, financial condition, and future success.

# We are subject to federal, state and foreign healthcare laws and regulations and implementation or changes to such healthcare laws and regulations could adversely affect our business and results of operations.

In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory proposals in recent years to change the healthcare system in ways that could impact our ability to sell our potential products profitably, described in greater detail in the Government Regulation section of this Report. If we are found to be in violation of any of these laws or any other federal or state regulations, we may be subject to civil and/or criminal penalties, damages, fines, exclusion from federal health care programs and the restructuring of our operations. Any of these could have a material adverse effect on our business and financial results. Since many of these laws have not been fully interpreted by the courts, there is an increased risk that we may be found in violation of one or more of their provisions. Any action against us for violation of these laws, even if we ultimately are successful in our defense, will cause us to incur significant legal expenses and divert our management's attention away from the operation of our business.

In addition, in many foreign countries, particularly the countries of the European Union, the pricing of prescription drugs is subject to government control. In some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from

country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. We may face competition from lower-priced products in foreign countries that have placed price controls on pharmaceutical products. In addition, there may be importation of foreign products that compete with any products we may market, which could negatively impact our profitability.

We expect that the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we may receive for any approved product. An expansion in the government's role in the U.S. healthcare industry may cause general downward pressure on the prices of prescription drug products, lower reimbursements for providers using our products, reduce product utilization and adversely affect our business and results of operations. It is unclear whether and to what extent, if at all, other anticipated developments resulting from the federal healthcare reform legislation, such as an increase in the number of people with health insurance and an increased focus on preventive medicine, may provide us additional revenue to offset the annual excise tax on certain drug product sales enacted under the ACA, subject to limited exceptions. It is possible that the tax burden, if we are not excepted, would adversely affect our financial performance, which in turn could cause the price of our stock to decline. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize any products for which we receive regulatory approval.

# If we receive marketing approval from the FDA, we could face liability if a regulatory authority determines that we are promoting "off-label" use of our products.

A company may not promote "off-label" uses for its drug products. An off-label use is the use of a product for an indication that is not described in the product's FDA-approved label or for uses that differ from those approved by other applicable regulatory agencies. Physicians, on the other hand, may prescribe products for off-label uses. Although the FDA and other regulatory agencies do not regulate a physician's choice of drug treatment, they do restrict promotional communications from pharmaceutical companies or their sales force with respect to off-label uses of products for which marketing clearance has not been issued. A company that is found to have promoted off-label use of its product may be subject to significant liability, including civil and criminal sanctions. If we begin marketing any product, we intend to comply with the FDA and other regulatory agencies with respect to our promotion of our products, but we cannot be sure that the FDA or other regulatory agencies will agree that we have not violated their restrictions. As a result, we may be subject to criminal and civil liability. In addition, our management's attention could be diverted to handle any such alleged violations.

# If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market any products we may develop, we may not be able to generate product revenues.

While we have begun to establish a small commercial team, we do not currently have a complete organization for the sales, marketing and distribution of pharmaceutical products. In order to market any products that may be approved by the FDA, we must build our sales, marketing, managerial, and related capabilities or make arrangements with third parties to perform these services. If we are unable to establish adequate sales, marketing, and distribution capabilities, whether independently or with third parties, we may not be able to generate product revenues and may not become profitable.

# We will need to obtain FDA approval of our proposed product name for pimavanserin, and the failure or any delay in receiving this approval may adversely impact the timing and success of our sales and marketing efforts.

The FDA will need to approve any product name we intend to use for pimavanserin regardless of whether we have obtained a formal trademark registration from the United States Patent and Trademark Office. Typically,

the FDA conducts an extensive review of proposed product names, including an evaluation for possible confusion with other existing product names. If the FDA objects to our proposed name, we will need to adopt an alternative name. As a result, we would lose the benefit of any existing trademark applications and may need to spend significant resources in an effort to select another product name that will meet FDA approval, qualify under existing trademark laws and not infringe on the existing rights of third parties. In addition, we will need to develop brand loyalty for any product name in order to commercialize pimavanserin effectively. If we fail to do this, it could negatively impact our future revenues from sales of pimavanserin.

# If we engage in any acquisition, we will incur a variety of costs and may never realize the anticipated benefits of the acquisition.

We may attempt to acquire, or license in, businesses, technologies, product candidates or products that we believe are a strategic fit with our business. We have limited experience in identifying acquisition targets, successfully completing proposed acquisitions and integrating any acquired businesses, technologies, services or products into our current infrastructure. The process of integrating any acquired business, technology, service, or product may result in unforeseen operating difficulties and expenditures and may divert significant management attention from our ongoing business operations. As a result, we will incur a variety of costs in connection with an acquisition and may never realize its anticipated benefits.

# Earthquake or fire damage to our facilities could delay our research and development efforts and adversely affect our business.

Our headquarters and research and development facilities in San Diego are located in a seismic zone, and there is the possibility of an earthquake, which could be disruptive to our operations and result in delays in our research and development efforts. In addition, while our facilities have not been adversely impacted by local wildfires, there is the possibility of future fires in the area. In the event of an earthquake or fire, if our facilities or the equipment in our facilities is significantly damaged or destroyed for any reason, we may not be able to rebuild or relocate our facilities or replace any damaged equipment in a timely manner and our business, financial condition, and results of operations could be materially and adversely affected. We do not have insurance for damages resulting from earthquakes. While we do have fire insurance for our property and equipment located in San Diego, any damage sustained in a fire could cause a delay in our research and development efforts and our results of operations could be materially and adversely affected.

#### Risks Related to Our Intellectual Property

### Our ability to compete may decline if we do not adequately protect our proprietary rights.

Our commercial success depends on obtaining and maintaining proprietary rights to our product candidates and technologies and their uses, as well as successfully defending these rights against third-party challenges. We will only be able to protect our product candidates, proprietary technologies, and their uses from unauthorized use by third parties to the extent that valid and enforceable patents, or effectively protected trade secrets, cover them. Although we have filed numerous patent applications worldwide with respect to pimavanserin, we have not been issued patents with respect to each of our filings.

Our ability to obtain patent protection for our product candidates and technologies is uncertain due to a number of factors, including:

- we may not have been the first to make the inventions covered by our pending patent applications or issued patents;
- we may not have been the first to file patent applications for our product candidates or the technologies we rely upon;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;

- our disclosures in patent applications may not be sufficient to meet the statutory requirements for patentability;
- any or all of our pending patent applications may not result in issued patents;
- we may not seek or obtain patent protection in all countries that will eventually provide a significant business opportunity;
- any patents issued to us or our collaborators may not provide a basis for commercially viable products, may not provide us with any competitive advantages or may be challenged by third parties;
- our proprietary technologies may not be patentable;
- others may design around our patent claims to produce competitive products which fall outside of the scope of our patents;
- · others may identify prior art which could invalidate our patents; or
- changes to patent laws that limit the exclusivity rights of patent holders.

Even if we have or obtain patents covering our product candidates or technologies, we may still be barred from making, using and selling our product candidates or technologies because of the patent rights of others. Others have or may have filed, and in the future are likely to file, patent applications covering compounds, assays, genes, gene products or therapeutic products that are similar or identical to ours. There are many issued U.S. and foreign patents relating to genes, nucleic acids, polypeptides, chemical compounds or therapeutic products, and some of these may encompass reagents utilized in the identification of candidate drug compounds or compounds that we desire to commercialize. Numerous U.S. and foreign issued patents and pending patent applications owned by others exist in the area of central nervous system disorders and the other fields in which we are developing products. These could materially affect our ability to develop our product candidates or sell our products. Because patent applications can take many years to issue, there may be currently pending applications, unknown to us, that may later result in issued patents that our product candidates or technologies may infringe. These patent applications may have priority over patent applications filed by us.

We regularly conduct searches to identify patents or patent applications that may prevent us from obtaining patent protection for our proprietary compounds or that could limit the rights we have claimed in our patents and patent applications. Disputes may arise regarding the ownership or inventorship of our inventions. It is difficult to determine how such disputes would be resolved. Others may challenge the validity of our patents. If our patents are found to be invalid, we will lose the ability to exclude others from making, using or selling the inventions claimed therein.

Some of our academic institutional licensors, research collaborators and scientific advisors have rights to publish data and information to which we have rights. If we cannot maintain the confidentiality of our technology and other confidential information in connection with our collaborations, then our ability to receive patent protection or protect our proprietary information will be impaired. Additionally, former employees of ours may seek future employment with our competitors. Although each of our employees is required to sign a confidentiality agreement with us at the time of hire, we cannot guarantee that the confidential nature of our proprietary information will be maintained in the course of such future employment. In addition, technology that we may license in may become important to some aspects of our business. We generally will not control the patent prosecution, maintenance or enforcement of in-licensed technology.

Confidentiality agreements with employees and others may not adequately prevent disclosure of our trade secrets and other proprietary information and may not adequately protect our intellectual property, which could limit our ability to compete.

Because we operate in the highly technical field of drug discovery and development of small molecule drugs, we rely in part on trade secret protection in order to protect our proprietary technology and processes.

However, trade secrets are difficult to protect. We enter into confidentiality and intellectual property assignment agreements with our corporate partners, employees, consultants, outside scientific collaborators, sponsored researchers, and other advisors. These agreements generally require that the other party keep confidential and not disclose to third parties all confidential information developed by the party or made known to the party by us during the course of the party's relationship with us. These agreements also generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us. Enforcing a claim that a party illegally obtained and is using our trade secrets is difficult, expensive and time consuming and the outcome is unpredictable. In addition, courts outside the United States may be less willing to protect trade secrets. The failure to obtain or maintain trade secret protection could adversely affect our competitive position. In addition, we have not entered into any noncompete agreements with any of our employees.

# A dispute concerning the infringement or misappropriation of our proprietary rights or the proprietary rights of others could be time consuming and costly, and an unfavorable outcome could harm our business.

There is significant litigation in our industry regarding patent and other intellectual property rights. While we are not currently subject to any pending intellectual property litigation, and are not aware of any such threatened litigation, we may be exposed to future litigation by third parties based on claims that our product candidates, technologies or activities infringe the intellectual property rights of others. In particular, there are many patents relating to specific genes, nucleic acids, polypeptides or the uses thereof to identify product candidates. Some of these may encompass genes or polypeptides that we utilize in our drug development activities. If our drug development activities are found to infringe any such patents, we may have to pay significant damages or seek licenses to such patents. A patentee could prevent us from using the patented genes or polypeptides for the identification or development of drug compounds. There are also many patents relating to chemical compounds and the uses thereof. If our compounds are found to infringe any such patents, we may have to pay significant damages or seek licenses to such patents. A patentee could prevent us from making, using or selling the patented compounds. We may need to resort to litigation to enforce a patent issued to us, protect our trade secrets or determine the scope and validity of third-party proprietary rights. From time to time, we may hire scientific personnel formerly employed by other companies involved in one or more areas similar to the activities conducted by us. Either we or these individuals may be subject to allegations of trade secret misappropriation or other similar claims as a result of their prior affiliations. If we become involved in litigation, it could consume a substantial portion of our managerial and financial resources, regardless of whether we win or lose. We may not be able to afford the costs of litigation. Any legal action against us or our collaborators could lead to:

- payment of damages, potentially treble damages, if we are found to have willfully infringed a party's patent rights;
- injunctive or other equitable relief that may effectively block our ability to further develop, commercialize, and sell products; or
- we or our collaborators having to enter into license arrangements that may not be available on commercially acceptable terms, if at all.

As a result, we could be prevented from commercializing current or future products.

# The patent applications of pharmaceutical and biotechnology companies involve highly complex legal and factual questions, which, if determined adversely to us, could negatively impact our patent position.

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions. For example, some of our patent applications will cover gene sequences and products and the uses of those gene sequences and products. Public disclosures and patent applications related to the Human Genome Project and other genomics efforts may limit the scope of our claims or make unpatentable subsequent patent applications. No consistent policy regarding the breadth of claims allowed in biotechnology patents has emerged to date. The U.S. Patent and Trademark Office's standards are uncertain and could change in

the future. Consequently, the issuance and scope of patents cannot be predicted with certainty. Patents, if issued, may be challenged, invalidated or circumvented. U.S. patents and patent applications may also be subject to interference proceedings, and U.S. patents may be subject to reexamination proceedings in the U.S. Patent and Trademark Office (and foreign patents may be subject to opposition or comparable proceedings in the corresponding foreign patent office), which proceedings could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. Similarly, opposition or invalidity proceedings could result in loss of rights or reduction in the scope of one or more claims of a patent in foreign jurisdictions. In addition, such interference, reexamination and opposition proceedings may be costly. Accordingly, rights under any issued patents may not provide us with sufficient protection against competitive products or processes.

In addition, changes in or different interpretations of patent laws in the United States and foreign countries may permit others to use our discoveries or to develop and commercialize our technology and products without providing any compensation to us or may limit the number of patents or claims we can obtain. In particular, there have been proposals to shorten the exclusivity periods available under U.S. patent law that, if adopted, could substantially harm our business. The product candidates that we are developing are protected by intellectual property rights, including patents and patent applications. If any of our product candidates becomes a marketable product, we will rely on our exclusivity under patents to sell the compound and recoup our investments in the research and development of the compound. If the exclusivity period for patents is shortened, then our ability to generate revenues without competition will be reduced and our business could be materially adversely impacted. The laws of some countries do not protect intellectual property rights to the same extent as U.S. laws and those countries may lack adequate rules and procedures for defending our intellectual property rights. For example, some countries, including many in Europe, do not grant patent claims directed to methods of treating humans and, in these countries, patent protection may not be available at all to protect our product candidates. In addition, U.S. patent laws may change which could prevent or limit us from filing patent applications or patent claims to protect our products and/or technologies or limit the exclusivity periods that are available to patent holders. For example, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was recently signed into law and includes a number of significant changes to U.S. patent law. These include changes to transition from a "first-to-invent" system to a "first-to-file" system and to the way issued patents are challenged. These changes may favor larger and more established companies that have more resources to devote to patent application filing and prosecution. The U.S. Patent and Trademark Office has been in the process of implementing regulations and procedures to administer the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act may affect our ability to obtain, enforce or defend our patents. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will ultimately have on the cost of prosecuting our patent applications, our ability to obtain patents based on our discoveries and our ability to enforce or defend our issued patents.

If we fail to obtain and maintain patent protection and trade secret protection of our product candidates, proprietary technologies and their uses, we could lose our competitive advantage and competition we face would increase, reducing our potential revenues and adversely affecting our ability to attain or maintain profitability.

### **Risks Related to Our Industry**

We will be subject to stringent regulation in connection with the marketing of any products derived from our product candidates, which could delay the development and commercialization of our products.

The pharmaceutical industry is subject to stringent regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Neither we nor our collaborators can market a pharmaceutical product in the United States until it has completed rigorous preclinical testing and clinical trials and an extensive regulatory clearance process implemented by the FDA. Satisfaction of regulatory requirements typically takes many years, depends upon the type, complexity and novelty of the product, and requires substantial resources. Even if regulatory approval is obtained, it may impose significant restrictions on the indicated uses, conditions for use, labeling, advertising, promotion, and/or marketing of such products, and requirements for post-approval studies, including additional research and development and clinical trials. These

limitations may limit the size of the market for the product or result in the incurrence of additional costs. Any delay or failure in obtaining required approvals could have a material adverse effect on our ability to generate revenues from the particular product candidate.

Outside the United States, the ability to market a product is contingent upon receiving approval from the appropriate regulatory authorities. The requirements governing the conduct of clinical trials, marketing authorization, pricing, and reimbursement vary widely from country to country. Only after the appropriate regulatory authority is satisfied that adequate evidence of safety, quality, and efficacy has been presented will it grant a marketing authorization. Approval by the FDA does not automatically lead to the approval by regulatory authorities outside the United States will not automatically lead to FDA approval.

In addition, U.S. and foreign government regulations control access to and use of some human or other tissue samples in our research and development efforts. U.S. and foreign government agencies may also impose restrictions on the use of data derived from human or other tissue samples. Accordingly, if we fail to comply with these regulations and restrictions, the commercialization of our product candidates may be delayed or suspended, which may delay or impede our ability to generate product revenues.

# If our competitors develop and market products that are more effective than our product candidates, they may reduce or eliminate our commercial opportunity.

Competition in the pharmaceutical and biotechnology industries is intense and expected to increase. We face competition from pharmaceutical and biotechnology companies, as well as numerous academic and research institutions and governmental agencies, both in the United States and abroad. Some of these competitors have products or are pursuing the development of drugs that target the same diseases and conditions that are the focus of our drug development programs.

For example, the use of pimavanserin for PDP would compete with off-label use of antipsychotic drugs, including Seroquel, marketed by Astra-Zeneca, and with the generic drug clozapine. Our potential products for the treatment of schizophrenia would compete with Zyprexa, marketed by Eli Lilly, Risperdal, marketed by Johnson & Johnson, Abilify, marketed jointly by Bristol-Myers Squibb and Otsuka Pharmaceutical, Seroquel, and clozapine. Our potential product for ADP would compete with Risperdal and with off-label use of antipsychotic drugs. In the area of chronic pain, potential products would compete with Lyrica, marketed by Pfizer, and Cymbalta, marketed by Eli Lilly, as well as a variety of generic or proprietary opioids. Our potential products for the treatment of glaucoma would compete with Xalatan, marketed by Pfizer, and Lumigan and Alphagan, marketed by Allergan.

Many of our competitors and their collaborators have significantly greater experience than we do in the following:

- identifying and validating targets;
- screening compounds against targets;
- preclinical studies and clinical trials of potential pharmaceutical products; and
- obtaining FDA and other regulatory approvals.

In addition, many of our competitors and their collaborators have substantially greater capital and research and development resources, manufacturing, sales and marketing capabilities, and production facilities. Smaller companies also may prove to be significant competitors, particularly through proprietary research discoveries and collaboration arrangements with large pharmaceutical and established biotechnology companies. Many of our competitors have products that have been approved or are in advanced development and may develop superior technologies or methods to identify and validate drug targets and to discover novel small molecule drugs. Our competitors, either alone or with their collaborators, may succeed in developing drugs that are more effective,

safer, more affordable, or more easily administered than ours and may achieve patent protection or commercialize drugs sooner than us. Our competitors may also develop alternative therapies that could further limit the market for any drugs that we may develop. Our failure to compete effectively could have a material adverse effect on our business.

# Any claims relating to improper handling, storage, or disposal of biological, hazardous, and radioactive materials used in our business could be costly and delay our research and development efforts.

Our research and development activities involve the controlled use of potentially harmful hazardous materials, including volatile solvents, biological materials such as blood from patients that has the potential to transmit disease, chemicals that cause cancer, and various radioactive compounds. Our operations also produce hazardous waste products. We face the risk of contamination or injury from the use, storage, handling or disposal of these materials. We are subject to federal, state and local laws and regulations governing the use, storage, handling, and disposal of these materials and specified waste products. The cost of compliance with these laws and regulations could be significant, and current or future environmental regulations may impair our research, development, or production efforts. If one of our employees were accidentally injured from the use, storage, handling, or disposal of these materials, the medical costs related to his or her treatment would be covered by our workers' compensation insurance policy. However, we do not carry specific biological or hazardous waste insurance coverage and our general liability insurance policy specifically excludes coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be subject to criminal sanctions or fines or be held liable for damages, our operating licenses could be revoked, or we could be required to suspend or modify our operations and our research and development efforts.

# Consumers may sue us for product liability, which could result in substantial liabilities that exceed our available resources and damage our reputation.

Researching, developing, and commercializing drug products entails significant product liability risks. Liability claims may arise from our and our collaborators' use of products in clinical trials and the commercial sale of those products. Consumers may make these claims directly and our collaborators or others selling these products may seek contribution from us if they receive claims from consumers. Although we currently have product liability insurance that covers our clinical trials, we will need to increase and expand this coverage if we commence larger scale trials and if our product candidates are approved for commercial sale. 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 inhibit the commercialization of products that we or our collaborators develop. Product liability claims could have a material adverse effect on our business and results of operations. Our liability could exceed our total assets if we do not prevail in a lawsuit from any injury caused by our drug products.

#### Risks Related to Our Common Stock

### Our stock price may be particularly volatile because we are a drug discovery and development company.

The market prices for securities of biotechnology companies in general, and drug discovery and development companies in particular, have been highly volatile and may continue to be highly volatile in the future. The following factors, in addition to other risk factors described in this section, may have a significant impact on the market price of our common stock:

- the development status of our product candidates, including results of development and commercialization efforts in our pimavanserin development program or our chronic pain or glaucoma collaborations;
- the timing, or developments regarding the timing, of submission and review of filings for our product candidates for approval by regulatory authorities in the United States and abroad and the results of any applications for marketing approval of product candidates;

- any other communications or guidance from the FDA or other regulatory authorities that pertain to our product candidates, including pimavanserin;
- the initiation, termination, or reduction in the scope of our collaborations or any disputes or developments regarding our collaborations;
- market conditions or trends related to biotechnology and pharmaceutical industries, or the market in general;
- announcements of technological innovations, new commercial products, or other material events by our competitors or us;
- disputes or other developments concerning our proprietary and intellectual property rights;
- changes in, or failure to meet, securities analysts' or investors' expectations of our financial performance;
- our failure to meet applicable NASDAQ listing standards and the possible delisting of our common stock from the NASDAQ Global Market;
- additions or departures of key personnel;
- discussions of our business, products, financial performance, prospects, or stock price by the financial and scientific press and online investor communities such as blogs and chat rooms;
- public concern as to, and legislative action with respect to, genetic testing or other research areas of biopharmaceutical companies, the pricing and availability of prescription drugs, or the safety of drugs and drug delivery techniques;
- regulatory developments in the United States and in foreign countries;
- the announcement of, or developments in, any litigation matters; and
- economic and political factors, including but not limited to economic and financial crises, wars, terrorism, and political unrest.

In particular, our development program with pimavanserin encompasses a number of studies, open-label safety extension trials and a range of supporting studies, such as drug-drug interaction studies and CMC development, including stability testing of registration batches. Any unfavorable outcome in one or more of the studies in the development of pimavanserin, or the CMC development related thereto, could be a major set-back for our company, generally. Such an unfavorable outcome could have a material adverse effect on our company and the value of our common stock.

In the past, following periods of volatility in the market price of a particular company's securities, securities class action litigation has often been brought against that company. We may become subject to this type of litigation, which is often extremely expensive and diverts management's attention.

# If we or our stockholders sell substantial amounts of our common stock, the market price of our common stock may decline.

A significant number of shares of our common stock are held by a small number of stockholders. Sales of a significant number of shares of our common stock, or the expectation that such sales may occur, could significantly reduce the market price of our common stock. We filed registration statements in connection with private financings that we concluded in January 2011 and December 2012, which registrations cover approximately 17.0 million shares and 19.5 million shares of our common stock, respectively. We also have an effective registration statement to sell shares of our common stock on our own behalf, and may elect to sell shares pursuant to such registration, or pursuant to a new registration statement or in a private placement, from time to time. Our stock price may decline as a result of the sale of the shares of our common stock included in any of these registration statements or future financings.

If our officers, directors, and largest stockholders choose to act together, they may be able to significantly influence our management and operations, acting in their best interests and not necessarily those of our other stockholders.

Our directors, executive officers and holders of five percent or more of our outstanding common stock and their affiliates beneficially own a substantial portion of our outstanding common stock. As a result, these stockholders, acting together, have the ability to significantly influence all matters requiring approval by our stockholders, including the election of all of our board members, amendments to our certificate of incorporation, going-private transactions, and the approval of mergers or other business combination transactions. The interests of this group of stockholders may not always coincide with the company's interests or the interests of other stockholders and they may act in a manner that advances their best interests and not necessarily those of our other stockholders.

# Anti-takeover provisions in our charter documents and under Delaware law may make an acquisition of us more complicated and may make the removal and replacement of our directors and management more difficult.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that may delay or prevent a change in control, discourage bids at a premium over the market price of our common stock and adversely affect the market price of our common stock and the voting and other rights of the holders of our common stock. These provisions may also make it difficult for stockholders to remove and replace our board of directors and management. These provisions:

- establish that members of the board of directors may be removed only for cause upon the affirmative vote of stockholders owning at least a majority of our capital stock;
- authorize the issuance of "blank check" preferred stock that could be issued by our board of directors to increase the number of outstanding shares and prevent or delay a takeover attempt;
- limit who may call a special meeting of stockholders;
- establish advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings;
- prohibit our stockholders from making certain changes to our amended and restated certificate of incorporation or amended and restated bylaws except with 66 <sup>2</sup>/<sub>3</sub> percent stockholder approval; and
- provide for a board of directors with staggered terms.

We are also subject to provisions of the Delaware corporation law that, in general, prohibit any business combination with a beneficial owner of 15 percent or more of our common stock for three years unless the holder's acquisition of our stock was approved in advance by our board of directors. Although we believe these provisions collectively provide for an opportunity to receive higher bids by requiring potential acquirors to negotiate with our board of directors, they would apply even if the offer may be considered beneficial by some stockholders.

### Adverse securities and credit market conditions may significantly affect our ability to raise capital.

Historically, turmoil and volatility in the financial markets have adversely affected the market capitalizations of many biotechnology companies, and generally made equity and debt financing more difficult to obtain. These events, coupled with other factors, may limit our access to financing in the future. This could have a material adverse effect on our ability to access funding on acceptable terms, or at all, and our stock price may suffer further as a result.

We do not intend to pay dividends on our common stock in the foreseeable future; as such, you must rely on stock appreciation for any return on your investment.

To date, we have not paid any cash dividends on our common stock, and we do not intend to pay any dividends in the foreseeable future. Instead, we intend to retain any future earnings to fund the development and

growth of our business. For this reason, the success of an investment in our common stock, if any, will depend on the appreciation of our common stock, which may not occur. There is no guarantee that our common stock will appreciate, and therefore, a holder of our common stock may not realize a return on his or her investment.

### Item 1B. Unresolved Staff Comments.

This item is not applicable.

### Item 2. Properties.

Our primary facility consists of approximately 19,000 square feet of leased office space located in San Diego, California, which is leased through the end of 2016 with an option to extend. We also lease two other facilities in San Diego related to our research and development activities that cover an aggregate of approximately 11,000 square feet of laboratory and office space. We believe that our existing facilities are adequate for our current needs.

### Item 3. Legal Proceedings.

This item is not applicable.

### Item 4. Mine Safety Disclosures.

This item is not applicable.

### **PART II**

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

(a) Our common stock is traded on the NASDAQ Global Market under the symbol "ACAD". The following table sets forth the high and low sale prices for our common stock as reported on the NASDAQ Global Market for the periods indicated.

2013	High	Low
First Quarter	\$ 8.81	\$ 4.60
Second Quarter	\$20.09	\$ 7.40
Third Quarter	\$28.38	\$17.02
Fourth Quarter	\$29.73	\$19.65
2012	High	Low
2012 First Quarter	High \$ 2.30	Low \$ 1.07
First Quarter	\$ 2.30	\$ 1.07

As of February 13, 2014, there were approximately 46 stockholders of record of our common stock. We have not paid any cash dividends to date and do not anticipate any being paid in the foreseeable future.

#### Item 6. Selected Financial Data.

The following data has been derived from our audited financial statements, including the consolidated balance sheets at December 31, 2013 and 2012 and the related consolidated statements of operations for the three years ended December 31, 2013 and related notes appearing elsewhere in this report. The statement of operations data for the years ended December 31, 2010 and 2009 and the balance sheet data as of December 31, 2011, 2010 and 2009 are derived from our audited consolidated financial statements that are not included in this report. You should read the selected financial data set forth below in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and related notes included elsewhere in this report.

	Years Ended December 31,				
	2013	2012	2011	2010 (1)	2009
		(in thousand	s, except per	share data)	
Consolidated Statement of Operations Data:					
Revenues:					
Collaborative revenues	\$ 1,145	\$ 4,907	\$ 2,067	\$42,135	\$ 6,399
Operating expenses:					
Research and development	26,722	18,794	17,309	20,579	41,585
General and administrative	12,720	6,999	7,610	6,462	10,282
Total operating expenses	39,442	25,793	24,919	27,041	51,867
Income (loss) from operations	(38,297)	(20,886)	(22,852)	15,094	(45,468)
Interest income, net	349	37	87	45	323
Net income (loss)	\$(37,948)	\$(20,849)	\$(22,765)	\$15,139	\$(45,145)
Net income (loss) per common share, basic	\$ (0.44)	\$ (0.38)	\$ (0.44)	\$ 0.39	\$ (1.20)
Net income (loss) per common share, diluted	\$ (0.44)	\$ (0.38)	\$ (0.44)	\$ 0.39	\$ (1.20)
Weighted average shares used in computing net income			·	·	
(loss) per common share, basic	85,715	55,116	52,183	38,593	37,476
Weighted average shares used in computing net income					
(loss) per common share, diluted	85,715	55,116	52,183	38,720	37,476

<sup>(1)</sup> In October 2010, we ended our collaboration and license agreement with Biovail Laboratories International SRL and recognized all remaining revenues related to this collaboration, resulting in net income for us in the year ended December 31, 2010.

	At December 31,				
	2013	2012	2011	2010	2009
	(in thousands)				
Consolidated Balance Sheet Data:					
Cash, cash equivalents and investment securities	\$185,790	\$107,967	\$31,048	\$37,087	\$47,060
Working capital	181,381	102,600	25,784	31,890	33,766
Total assets	189,118	108,590	32,114	38,394	49,680
Long-term debt, less current portion	_	_	_	32	98
Total stockholders' equity	182,131	84,984	23,362	29,688	12,114

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

The following discussion and analysis of our consolidated financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes included elsewhere in this report. Past operating results are not necessarily indicative of results that may occur in future periods. This discussion contains forward-looking statements, which involve a number of risks and uncertainties. Such forward-looking statements include statements about our strategies, objectives, expectations, discoveries, collaborations, clinical trials, proprietary and external programs, products or product candidates, and other statements that are not historical facts, including statements which may be preceded by the words "believes," "expects," "hopes," "may," "will," "plans," "intends," "estimates," "could," "should," "would," "continue," "seeks," "aims," "projects," "prodicts," "pro forma," "anticipates," "potential" or similar words. For forward-looking statements, we claim the protection of the Private Securities Litigation Reform Act of 1995. Readers of this report are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date on which they are made. We undertake no obligation to update or revise publicly any forward-looking statements. Forward-looking statements are not guarantees of performance. Actual results or events may differ materially from those anticipated in our forward-looking statements as a result of various factors, including those set forth under the section captioned "Risk Factors" elsewhere in this report. Information in the following discussion for a yearly period means for the year ended December 31 of the indicated year.

### Overview

#### **Background**

We are a biopharmaceutical company focused on the development and commercialization of innovative small molecule drugs that address unmet medical needs in neurological and related central nervous system disorders. We have a pipeline of product candidates led by pimavanserin, which is in Phase III development for Parkinson's disease psychosis and has the potential to be the first drug approved in the United States for this disorder. Pimavanserin is also in Phase II development for Alzheimer's disease psychosis and has successfully completed a Phase II trial as a co-therapy for schizophrenia. We hold worldwide commercialization rights to pimavanserin. Our pipeline also includes clinical-stage programs for chronic pain and glaucoma in collaboration with Allergan, Inc., and two advanced preclinical programs directed at Parkinson's disease and other neurological disorders. All of our product candidates and programs emanate from internal discoveries.

We are pursuing Parkinson's disease psychosis as our lead indication for pimavanserin. We have completed a successful pivotal Phase III trial with pimavanserin in patients with Parkinson's disease psychosis, the -020 Study. Following this study, we met with the FDA and announced that the agency agreed that the data from the -020 Study, together with supportive data from our other studies with pimavanserin, are sufficient to support the filing of an NDA for the treatment of Parkinson's disease psychosis. We are currently completing the remaining aspects of our development program that are needed for submission of this NDA. Subject to changes that could result from future interactions with the FDA or other developments, we are planning to submit the NDA near the end of 2014. If approved, we intend to commercialize pimavanserin for this indication in the United States by establishing a specialty sales force. We believe that pimavanserin also has the potential to address a range of other neurological and psychiatric disorders, including Alzheimer's disease psychosis and schizophrenia. We are currently conducting a Phase II trial to examine the efficacy and safety of pimavanserin as a treatment for patients with Alzheimer's disease psychosis. We have completed a successful Phase II trial with pimavanserin as a co-therapy for schizophrenia and we are currently planning additional studies for this indication.

We have incurred substantial operating losses since our inception due in large part to expenditures for our research and development activities. As of December 31, 2013, we had an accumulated deficit of \$405.7 million. We expect to continue to incur operating losses for at least the next several years as we pursue the development and commercialization of our product candidates.

#### Revenues

We have not generated any revenues from product sales to date. Our revenues to date have been generated substantially from payments under our current and past collaboration agreements. As of December 31, 2013, we had received an aggregate of \$115.7 million in payments under these agreements, including upfront payments, research funding, milestone payments, and reimbursed development expenses. Until such time as we may complete development of, receive regulatory approval for, and generate product sales from pimavanserin or other products, we expect our revenues to be derived primarily from payments under our current agreements with Allergan and potential additional collaborations, as well as grant funding.

We have been a party to three collaboration agreements with Allergan, one of which concluded in March 2013. Our two ongoing collaboration agreements with Allergan involve the development of product candidates in the areas of chronic pain and glaucoma. We are eligible to receive payments upon achievement of development and regulatory milestones, as well as royalties on future product sales, if any, under each of our ongoing collaboration agreements with Allergan. However, we no longer receive research funding from these agreements and additional payments are dependent upon the advancement of our applicable product candidates. Each of our current agreements with Allergan is subject to termination upon notice by Allergan.

In March 2009, we entered into a collaboration agreement with Meiji Seika Pharma. In July 2012, we and Meiji Seika Pharma jointly decided to discontinue the development program that was being pursued under the collaboration, and the collaboration agreement was terminated pursuant to its terms. Upon the termination of this agreement and the end of our related performance obligations, we recorded as revenue all of the remaining deferred revenue from this collaboration during the third quarter of 2012.

#### Research and Development Expenses

Our research and development expenses have consisted primarily of fees paid to external service providers, salaries, and related personnel expenses, facilities and equipment expenses, and other costs. We charge all research and development expenses to operations as incurred. Our research and development activities are primarily focused on our most advanced product candidate, pimavanserin. We currently are responsible for all costs incurred in the development of pimavanserin as well as for the costs associated with our other internal programs. We are not responsible for, nor have we incurred, development expenses in our collaborative programs for chronic pain and glaucoma, which we are pursuing with Allergan.

We use external service providers to manufacture our product candidates and for the majority of the services performed in connection with the preclinical and clinical development of our product candidates. We have used our internal research and development resources, including our employees and discovery infrastructure, across several projects and many of our costs have not been attributable to a specific project. Accordingly, we have not reported our internal research and development costs on a project basis. To the extent that external expenses are not attributable to a specific project, they are included in other programs. The following table summarizes our research and development expenses for the years ended December 31, 2013, 2012, and 2011 (in thousands):

	Years Ended December 31,		
	2013	2012	2011
Costs of external service providers:			
Pimavanserin	\$16,625	\$12,401	\$10,373
Other programs	709	932	1,438
Subtotal	17,334	13,333	11,811
Internal costs	7,180	4,781	4,986
Stock-based compensation	2,208	680	512
Total research and development	\$26,722	\$18,794	\$17,309

While we intend to submit an NDA to the FDA for our lead program with pimavanserin near the end of 2014, at this time, due to the risks inherent in completing the development activities necessary to support the NDA and in regulatory and approval processes, we are unable to estimate with any certainty the costs we will incur for the continued development of pimavanserin for Parkinson's disease psychosis. Due to the risks inherent in clinical development, we also are unable to estimate with certainty the costs we will incur for the development of pimavanserin for other indications or for the development of our other product candidates. Due to these same factors, we are unable to determine with any certainty the anticipated completion dates for our current research and development programs. Clinical development and regulatory approval timelines, probability of success, and development costs vary widely. While our current focus is primarily on advancing the development of pimavanserin, we anticipate that we 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 of each product candidate's commercial potential and our financial position. We cannot forecast with any degree of certainty which product candidates will be subject to future collaborative or licensing arrangements, when such arrangements will be secured, if at all, and to what degree any such arrangements would affect our development plans and capital requirements.

We expect our research and development expenses to increase and continue to be substantial as we pursue the development of pimavanserin, including development and regulatory activities in our Phase III Parkinson's disease psychosis program, our Phase II trial in Alzheimer's disease psychosis, and potential studies in other indications, including schizophrenia, and the development of our other product candidates. The lengthy process of completing clinical trials and supporting development activities and seeking regulatory approval for our product candidates requires the expenditure of substantial resources. Any failure by us or delay in completing clinical trials, or in obtaining regulatory approvals, could cause our research and development expenses to increase and, in turn, have a material adverse effect on our results of operations.

#### General and Administrative Expenses

Our general and administrative expenses have consisted primarily of salaries and other costs for employees serving in executive, finance, business development, and business operations functions, as well as professional fees associated with legal and accounting services, and costs associated with patents and patent applications for our intellectual property. In addition, during 2013, we began establishing a small commercial organization that is designed to help prepare for the planned future launch of pimavanserin. We expect our general and administrative expenses to increase in future periods to support our planned development and commercial activities for pimavanserin and other product candidates.

#### **Critical Accounting Policies and Estimates**

Our discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements. We have identified the accounting policies that we believe require application of management's most subjective judgments, often requiring the need to make estimates about the effect of matters that are inherently uncertain and may change in subsequent periods. Our actual results may differ substantially from these estimates under different assumptions or conditions.

#### Revenue Recognition

We recognize revenues in accordance with authoritative guidance established by U.S. Generally Accepted Accounting Principles, or GAAP. Our revenues are primarily related to our collaboration agreements, which may provide for various types of payments to us, including upfront payments, funding of research and development, milestone payments, and licensing fees. Our collaboration agreements also include potential payments for product royalties; however, we have not received any product royalties to date.

We consider a variety of factors in determining the appropriate method of accounting under our collaboration agreements, including whether the various elements can be separated and accounted for

individually as separate units of accounting. Where there are multiple deliverables identified within a collaboration agreement that are combined into a single unit of accounting, revenues are deferred and recognized over the expected period of performance. The specific methodology for the recognition of the revenue is determined on a case-by-case basis according to the facts and circumstances of the applicable agreement.

Upfront, non-refundable payments that do not have stand-alone value are recorded as deferred revenue once received and recognized as revenues over the expected period of performance. Revenues from non-refundable license fees are recognized upon receipt of the payment if the license has stand-alone value, we do not have ongoing involvement or obligations, and we can determine the best estimate of the selling price for any undelivered items. When non-refundable license fees do not meet all of these criteria, the license revenues are recognized over the expected period of performance. Non-refundable payments for research funding are generally recognized as revenues over the period the related research activities are performed. Payments for reimbursement of external development costs are generally recognized as revenues using a contingency-adjusted performance model over the expected period of performance. Payments received from grants are recognized as revenues as the related research and development is performed and when collectability is reasonably assured.

We evaluate milestone payments on an individual basis and recognize revenues from non-refundable milestone payments when the earnings process is complete and collectability is reasonably assured. Non-refundable milestone payments related to arrangements under which we have continuing performance obligations are recognized as revenues upon achievement of the associated milestone, provided that (i) the milestone event is substantive and its achievability was not reasonably assured at the inception of the agreement and (ii) the amount of the milestone payment is reasonable in relation to the effort expended or the risk associated with the milestone event. Where separate milestone payments do not meet these criteria, we recognize revenue using a contingency-adjusted performance model over the expected period of performance.

### **Accrued Expenses**

We are required to estimate accrued expenses as part of our process of preparing financial statements. Examples of areas in which subjective judgments may be required include, among other things, costs associated with services provided by contract organizations for preclinical development, manufacturing of our product candidates, and clinical trials. We accrue for costs incurred as the services are being provided by monitoring the status of the trial or services provided, and the invoices received from our external service providers. In the case of clinical trials, a portion of the estimated cost normally relates to the projected cost to treat a patient in the trials, and this cost is recognized based on the number of patients enrolled in the trial. Other indirect costs are generally recognized on a straight-line basis over the estimated period of the study. As actual costs become known to us, we adjust our accruals. To date, our estimates have not differed materially from the actual costs incurred. However, subsequent changes in estimates may result in a material change in our accruals, which could also materially affect our balance sheet and results of operations.

#### Stock-Based Compensation

The fair value of each employee stock option and each employee stock purchase plan right granted is estimated on the grant date under the fair value method using the Black-Scholes model, which requires us to make a number of assumptions including the estimated expected life of the award and related volatility. The estimated fair values of stock options or purchase plan rights, including the effect of estimated forfeitures, are then expensed over the vesting period.

### **Results of Operations**

### Fluctuations in Operating Results

Our results of operations have fluctuated significantly from period to period in the past and are likely to continue to do so in the future. We anticipate that our quarterly and annual results of operations will be impacted

for the foreseeable future by several factors, including the timing and amount of payments received pursuant to our current and potential future collaborations, the progress and timing of expenditures related to our development and commercialization efforts, and the extent to which we generate revenues from product sales, if at all. Due to these fluctuations, we believe that the period-to-period comparisons of our operating results are not a good indication of our future performance.

#### Comparison of the Years Ended December 31, 2013 and 2012

#### Revenues

Revenues decreased to \$1.1 million in 2013 from \$4.9 million in 2012, primarily due to the termination of our collaboration with Meiji Seika Pharma in July 2012. We recognized a total of \$3.2 million in revenues from this collaboration in 2012. Revenues from our collaborations with Allergan decreased to \$571,000 in 2013 from \$1.1 million in 2012, primarily due to the conclusion of our 2003 research collaboration with Allergan in March 2013. Future revenues from our two ongoing collaboration agreements with Allergan are dependent upon the advancement of our applicable product candidates and we do not expect to receive significant revenues from these agreements unless and until a product is successfully developed and commercialized. Revenues from our agreements with other parties, including our research grants, totaled \$574,000 in 2013 compared to \$566,000 in 2012.

#### Research and Development Expenses

Research and development expenses increased to \$26.7 million in 2013, including \$2.2 million in stock-based compensation, from \$18.8 million in 2012, including \$680,000 in stock-based compensation. This increase was primarily due to an increase of \$4.0 million in external service costs as well as an increase in costs associated with our expanded research and development organization, including \$1.8 million in increased personnel costs, and \$1.5 million in increased stock-based compensation. External service costs totaled \$17.3 million, or 65 percent of our research and development expenses, in 2013, compared to \$13.3 million, or 71 percent of our research and development expenses, in 2012. The increase in external service costs was largely attributable to increased development costs incurred in our Phase III program for pimavanserin. We expect our research and development expenses to increase in future periods as we continue to pursue the development of pimavanserin, including our Phase III Parkinson's disease psychosis program, our Phase II trial for Alzheimer's disease psychosis, and potential studies in other indications, including schizophrenia, as well as the development of our other product candidates.

#### General and Administrative Expenses

General and administrative expenses increased to \$12.7 million in 2013, including \$3.5 million in stock-based compensation, from \$7.0 million in 2012, including \$1.3 million in stock-based compensation. The increase in general and administrative expenses was primarily due to an increase in costs associated with our expanded administrative organization, including \$2.3 million in increased stock-based compensation and \$1.2 million in increased personnel expenses, as well as an increase of \$1.6 million in external service costs. The increase in external service costs was largely attributable to increased professional fees, including initial costs related to our pre-commercial activities. We anticipate that our general and administrative expenses will increase in future periods to support our planned development and commercial activities for pimavanserin.

#### Comparison of the Years Ended December 31, 2012 and 2011

#### Revenues

Revenues increased to \$4.9 million in 2012 from \$2.1 million in 2011. This increase was primarily due to the termination of our collaboration with Meiji Seika Pharma in July 2012, at which time we recognized all of the remaining deferred revenue from this collaboration. We recognized a total of \$3.2 million in revenues from this

collaboration in 2012 compared to \$505,000 in 2011. Revenues from our collaborations with Allergan totaled \$1.1 million in each of 2012 and 2011. Revenues from our agreements with other parties, including our research and development grants, totaled \$566,000 in 2012 compared to \$486,000 in 2011.

### Research and Development Expenses

Research and development expenses increased to \$18.8 million in 2012, including \$680,000 in stock-based compensation, from \$17.3 million in 2011, including \$512,000 in stock-based compensation. The increase in research and development expenses was primarily due to \$1.5 million in increased external service costs as well as \$529,000 in increased salary and personnel costs offset, in part, by \$566,000 in decreased facility, equipment and other costs associated with our research and development organization. External service costs totaled \$13.3 million, or 71 percent of our research and development expenses, in 2012, compared to \$11.8 million, or 68 percent of our research and development expenses, in 2011. The increase in external service costs was largely attributable to increased clinical costs incurred in our Phase III program for pimavanserin offset, in part, by decreased costs of other programs.

#### General and Administrative Expenses

General and administrative expenses decreased to \$7.0 million in 2012, including \$1.3 million in stock-based compensation, from \$7.6 million in 2011, including \$1.1 million in stock-based compensation. The decrease in general and administrative expenses was primarily attributable to a net charge of \$1.1 million incurred during 2011 in connection with the termination of our Swedish facility lease offset, in part, by \$542,000 in increased salary and personnel costs in 2012.

### **Liquidity and Capital Resources**

Since inception, we have funded our operations primarily through sales of our equity securities, payments received under our collaboration agreements, debt financings, and interest income. As of December 31, 2013, we had received \$551.4 million in net proceeds from sales of our equity securities, including \$6.9 million in debt that we had retired through the issuance of our common stock, \$115.7 million in payments from collaboration agreements, \$22.4 million in debt financing, and \$22.6 million in interest income.

At December 31, 2013, we had \$185.8 million in cash, cash equivalents, and investment securities compared to \$108.0 million at December 31, 2012. We anticipate that the level of cash used in our operations will increase in 2014, relative to 2013, in order to fund our ongoing and planned development and precommercial activities for pimavanserin. We expect that our cash, cash equivalents, and investment securities will be greater than \$120 million at December 31, 2014, and that our cash resources will be sufficient to fund our operations at least through 2015.

We will require significant additional financing in the future to fund our operations. Our future capital requirements will depend on, and could increase significantly as a result of, many factors, including:

- the progress in, and the costs of, our development and pre-commercialization activities for pimavanserin and other research and development programs;
- the costs of preparing applications for regulatory approvals for our product candidates;
- the costs of establishing, or contracting for, sales and marketing capabilities for our product candidates.
- the scope, prioritization and number of research and development programs;
- the ability of our collaborators and us to reach the milestones or other events or developments triggering
  payments under our collaboration and licensing agreements, or our collaborators ability to make
  payments under these agreements;
- our ability to enter into new, and to maintain existing, collaboration and license agreements;

- the costs involved in filing, prosecuting, enforcing and defending patent claims and other intellectual property rights; and
- the costs of securing manufacturing arrangements for clinical or commercial production of product candidates.

Until we can generate significant continuing revenues, we expect to satisfy our future cash needs through strategic collaborations, public or private sales of our equity securities, debt financings, grant funding, or by licensing all or a portion of our product candidates or technology. We cannot be certain that adequate future funding will be available to us on acceptable terms, or at all. In the past, periods of turmoil and volatility in the financial markets have adversely affected the market capitalizations of many biotechnology companies and generally made equity and debt financing more difficult to obtain. These events, coupled with other factors, may limit our access to financing in the future. In particular, any unfavorable development in our pimavanserin program could have a material adverse effect on our ability to raise additional capital.

If we cannot raise adequate additional capital in the future, we will be required to delay, reduce the scope of, or eliminate one or more of our research or development programs or our commercialization efforts. We also may be required to relinquish greater or all rights to product candidates at an earlier stage of development or on less favorable terms than we would otherwise choose.

We have invested a substantial portion of our available cash in a money market fund, U.S. Treasury notes, and high quality, marketable debt instruments of corporations, financial institutions and government sponsored enterprises. We have adopted an investment policy and established guidelines relating to credit quality, diversification, and maturities of our investments to preserve principal and maintain liquidity. All investment securities have a credit rating of at least A3/A- or better, or P-1/A-1 or better, as determined by Moody's Investors Service or Standard & Poor's. Our investment portfolio has not been adversely impacted by the disruption in the credit markets that has occurred in the past. However, if there is future disruption in the credit markets, there can be no assurance that our investment portfolio will not be adversely affected in the future.

Net cash used in operating activities increased to \$31.8 million in 2013 compared to \$21.6 million in 2012 and \$19.9 million in 2011. The increase in net cash used in operating activities in 2013 relative to 2012 was primarily due to the increase in our net loss, offset by increases of \$3.8 million and \$1.7 million in non-cash stock-based compensation and amortization of premiums on investment securities, respectively, as well as by changes in our operating assets and liabilities, including prepaid expenses, receivables and other current assets, and deferred revenue. Prepaid expenses, receivables and other current assets increased by \$2.0 million in 2013 compared to a decrease of \$320,000 in 2012, primarily due to prepaid development costs and an increase in interest receivable on our investment securities. Deferred revenue decreased by \$379,000 during 2013 compared to a decrease of \$2.8 million in 2012. The decrease in deferred revenue in 2012 was primarily due to the termination of our collaboration with Meiji Seika Pharma in July 2012, at which time we recognized the remaining deferred revenue from this collaboration.

The increase in net cash used in operating activities in 2012 relative to 2011 was primarily due to changes in operating assets and liabilities, including a decrease in deferred revenue, and a non-cash charge in 2011 resulting from termination of our Swedish facility lease, offset by a decrease in our net loss. Deferred revenue decreased by \$2.8 million in 2012 compared to a decrease in deferred revenue of \$57,000 in 2011. The decrease in deferred revenue in 2012 was primarily due to the termination of our collaboration with Meiji Seika Pharma in July 2012.

Net cash used in investing activities totaled \$126.1 million in 2013 compared to net cash used in investing activities of \$25.5 million in 2012 and net cash provided by investing activities of \$6.0 in 2011. Net cash provided by or used in investing activities has fluctuated significantly from period to period primarily due to the timing of purchases and maturities of investment securities. The increase in net cash used in investing activities in 2013 relative to 2012 was primarily due to increased purchases of investment securities relative to maturities

of investment securities. The increase in net cash used in investing activities in 2012 relative to net cash provided by investing activities in 2011 was primarily due to increased purchases of investment securities and decreased maturities of investment securities.

Net cash provided by financing activities increased to \$111.7 million in 2013 compared to \$98.2 million in 2012 and \$13.9 million in 2011. The increase in net cash provided by financing activities in 2013 relative to 2012 was primarily attributable to increased proceeds from sales of our common stock and stock option exercises, which included \$107.9 million in net proceeds received from our public offering of common stock in May 2013. The increase in net cash provided by financing activities in 2012 relative to 2011 was primarily due to increased sales of our equity securities, which included \$80.5 million in net proceeds received from our December 2012 private equity financing as well as \$17.1 million in net proceeds received from the sale of common stock pursuant to an at-the-market issuance sales agreement.

The following table summarizes our contractual obligations at December 31, 2013 (in thousands):

We have also entered into agreements with contract research organizations and other external service providers for services, primarily in connection with the development of our product candidates. We were contractually obligated for up to approximately \$19.1 million of future services under these agreements as of December 31, 2013. The nature of the work being conducted under our agreements with contract research organizations is such that, in most cases, the services may be stopped on short notice. In such event, we would not be liable for the full amount of the contract. Our actual contractual obligations will vary depending upon several factors, including the progress and results of the underlying services.

In addition, we have entered into an agreement with the Ipsen Group pursuant to which we licensed certain intellectual property rights that complement our patent portfolio for our serotonin platform, including pimavanserin. If certain conditions are met, we would be required to make future payments, including milestones, sublicensing fees, and royalties. The amount of potential future milestone payments is \$10.5 million in the aggregate, which would be offset by any sublicensing fees we may pay under the agreement. Because these milestone payments would only be payable upon the achievement of specified regulatory events and it is uncertain when, or if, such events will occur, we cannot forecast with any degree of certainty when, or if, we will be required to make payments under the agreement. Accordingly, none of these amounts are included in the above table.

### Off-Balance Sheet Arrangements

To date, we have not had any relationships with unconsolidated entities or financial partnerships, such as entities referred to as structured finance or special purpose entities, which are established for the purpose of facilitating off-balance sheet arrangements or other contractually narrow or limited purposes. As such, we are not materially exposed to any financing, liquidity, market or credit risk that could arise if we had engaged in these relationships.

#### **Recent Accounting Pronouncements**

See Item 15 of Part IV, "Notes to Consolidated Financial Statements—Note 2—Summary of Significant Accounting Policies".

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

#### **Interest Rate Risk**

We invest our excess cash in investment-grade, interest-bearing securities. The primary objective of our investment activities is to preserve principal and liquidity. To achieve this objective, we invest in a money market fund, U.S. Treasury notes, and high quality marketable debt instruments of corporations, financial institutions and government sponsored enterprises with contractual maturity dates of generally less than two years. All investment securities have a credit rating of at least A3/A- or better, or P-1/A-1 or better, as determined by Moody's Investors Service or Standard & Poor's. We do not have any direct investments in auction-rate securities or securities that are collateralized by assets that include mortgages or subprime debt. If a 10 percent change in interest rates were to have occurred on December 31, 2013, this change would not have had a material effect on the fair value of our investment portfolio as of that date.

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

The consolidated financial statements required pursuant to this item are included in Item 15 of this report and are presented beginning on page F-1.

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

None.

#### Item 9A. Controls and Procedures.

#### Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our periodic and current reports that we file with the SEC is recorded, processed, summarized and reported within the time periods specified in the SEC'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 timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable and not absolute assurance of achieving the desired control objectives. In reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. In addition, the design of any system of controls is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, controls may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

As of December 31, 2013, we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2013.

#### Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is a process designed under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, to provide

reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States of America.

As of December 31, 2013, our management assessed the effectiveness of our internal control over financial reporting using the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control-Integrated Framework (1992). Based on this assessment, management, under the supervision and with the participation of our Chief Executive Officer and Chief Financial Officer, concluded that, as of December 31, 2013, our internal control over financial reporting was effective based on those criteria.

The effectiveness of our internal control over financial reporting as of December 31, 2013 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in its report, which appears under Item 15 in this Annual Report.

### Changes in Internal Control Over Financial Reporting

An evaluation was also performed under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of any change in our internal control over financial reporting that occurred during our last fiscal quarter and that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting. That evaluation did not identify any change in our internal control over financial reporting that occurred during our latest fiscal quarter and that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

#### **PART III**

### Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this Item and not set forth below will be set forth in the section headed "Proposal 1—Election of Directors" in our definitive Proxy Statement for our 2014 Annual Meeting of Stockholders to be filed with the SEC by April 30, 2014 (the "Proxy Statement") and is incorporated in this report by reference.

We have adopted a code of ethics for directors, officers (including our principal executive officer, principal financial officer and principal accounting officer) and employees, known as the Code of Business Conduct and Ethics. The Code of Business Conduct and Ethics is available on our website at <a href="http://www.acadia-pharm.com">http://www.acadia-pharm.com</a> under the Corporate Governance section of our Investors page. We will promptly disclose on our website (i) the nature of any amendment to the policy that applies to our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions and (ii) the nature of any waiver, including an implicit waiver, from a provision of the policy that is granted to one of these specified individuals, the name of such person who is granted the waiver and the date of the waiver. Stockholders may request a free copy of the Code of Business Conduct and Ethics from our corporate compliance officer, Glenn F. Baity c/o ACADIA Pharmaceuticals Inc., 11085 Torreyana Road, Suite 100, San Diego, CA 92121.

#### Item 11. Executive Compensation.

The information required by this Item will be set forth in the section headed "Executive Compensation" in our Proxy Statement and is incorporated in this report by reference.

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

The information required by this Item will be set forth in the section headed "Security Ownership of Certain Beneficial Owners and Management" in our Proxy Statement and is incorporated in this report by reference.

Information regarding our equity compensation plans will be set forth in the section headed "Executive Compensation" in our Proxy Statement and is incorporated in this report by reference.

### Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this Item will be set forth in the section headed "Transactions With Related Persons" in our Proxy Statement and is incorporated in this report by reference.

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

The information required by this Item will be set forth in the section headed "Proposal 3—Ratification of Selection of Independent Registered Public Accounting Firm" in our Proxy Statement and is incorporated in this report by reference.

### **PART IV**

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

- (a) Documents filed as part of this report.
- 1. The following financial statements of ACADIA Pharmaceuticals Inc. and Report of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm, are included in this report:

	Page Number
Report of Independent Registered Public Accounting Firm	F-1
Consolidated Balance Sheets at December 31, 2013 and 2012	F-2
Consolidated Statements of Operations for Each of the Three Years Ended December 31, 2013,	
2012, and 2011	F-3
Consolidated Statements of Comprehensive Loss for Each of the Three Years Ended December 31,	
2013, 2012, and 2011	F-4
Consolidated Statements of Cash Flows for Each of the Three Years Ended December 31, 2013,	
2012, and 2011	F-5
Consolidated Statements of Stockholders' Equity for Each of the Three Years Ended December 31,	
2013, 2012, and 2011	F-6
Notes to Consolidated Financial Statements	F-7

- 2. List of financial statement schedules. All schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.
  - 3. List of Exhibits required by Item 601 of Regulation S-K. See part (b) below.
  - (b) Exhibits. See the Exhibit Index and Exhibits filed as part of this report.

#### **SIGNATURES**

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

	/s/ Uli Hacksell	
Uli Hacksell, Ph.D.		
	Chief Executive Officer	

ACADIA PHARMACEUTICALS INC.

Date: February 27, 2014

KNOW ALL PERSONS BY THESE PRESENTS, that each individual whose signature appears below constitutes and appoints Uli Hacksell and Thomas H. Aasen, and each of them, his true and lawful attorneys-infact and agents with full power of substitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto and all 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 and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them, or his or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities and Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Uli Hacksell	Chief Executive Officer and Director	February 27, 2014
Uli Hacksell	(Principal Executive Officer)	
/s/ Thomas H. Aasen	Chief Financial Officer	February 27, 2014
Thomas H. Aasen	(Principal Financial Officer and Principal Accounting Officer)	
/s/ Leslie Iversen	Chairman of the Board	February 27, 2014
Leslie Iversen	_	
/s/ Stephen Biggar	Director	February 27, 2014
Stephen Biggar	_	
/s/ Michael Borer	Director	February 27, 2014
Michael Borer	_	
/s/ Laura Brege	Director	February 27, 2014
Laura Brege	_	
/s/ Mary Ann Gray	Director	February 27, 2014
Mary Ann Gray	_	
/s/ Lester Kaplan	Director	February 27, 2014
Lester Kaplan	_	
/s/ Torsten Rasmussen	Director	February 27, 2014
Torsten Rasmussen		
/s/ William M. Wells	Director	February 27, 2014
William M. Wells	_	,

#### REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of ACADIA Pharmaceuticals Inc.

In our opinion, the consolidated financial statements listed in the index appearing under Item 15(a)(1) present fairly, in all material respects, the financial position of ACADIA Pharmaceuticals Inc. and its subsidiaries at December 31, 2013 and 2012, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2013 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2013, based on criteria established in Internal Control—Integrated Framework (1992) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). The Company's management is responsible for these financial statements, for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Report on Internal Control over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on these financial statements and on the Company's internal control over financial reporting based on our integrated audit. 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 audits to obtain reasonable assurance about whether the financial statements are free of material misstatement and whether effective internal control over financial reporting was maintained in all material respects. Our audits of the financial statements included examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

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 (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) 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 (iii) 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.

/s/ PricewaterhouseCoopers LLP

San Diego, California February 27, 2014

### ACADIA PHARMACEUTICALS INC.

# CONSOLIDATED BALANCE SHEETS (in thousands, except for par value and share data)

	Decem	iber 31,	
	2013	2012	
Assets Cash and cash equivalents Investment securities, available-for-sale Prepaid expenses, receivables and other current assets	\$ 11,707 174,083 2,570	\$ 57,899 50,068 581	
Total current assets  Property and equipment, net  Other assets	188,360 579 179	108,548 42 —	
Total assets	\$ 189,118	\$ 108,590	
Liabilities, redeemable common stock and stockholders' equity  Accounts payable  Accrued expenses  Deferred revenue  Total current liabilities  Long-term liabilities  Total liabilities  Commitments and contingencies (Note 10)  Redeemable common stock, \$0.0001 par value; no shares and 5,347,137 shares issued	\$ 372 6,552 55 6,979 8 6,987	\$ 1,375 4,139 434 5,948 — 5,948	
and outstanding at December 31, 2013 and 2012, respectively (Note 7) Stockholders' equity  Preferred stock, \$0.0001 par value; 5,000,000 shares authorized at December 31, 2013 and 2012; no shares issued and outstanding at December 31, 2013 and 2012			
Additional paid-in capital	587,742	452,693	
Accumulated deficit	(405,668)	(367,720)	
Accumulated other comprehensive income	48	4	
Total stockholders' equity	182,131	84,984	
Total liabilities, redeemable common stock and stockholders' equity	\$ 189,118	\$ 108,590	

The accompanying notes are an integral part of these consolidated financial statements.

### ACADIA PHARMACEUTICALS INC.

### CONSOLIDATED STATEMENTS OF OPERATIONS

(in thousands, except per share data)

	Years Ended December 31,		
	2013	2012	2011
Revenues			
Collaborative revenues	\$ 1,145	\$ 4,907	\$ 2,067
Operating expenses Research and development (includes stock-based compensation of \$2,208,			
\$680, and \$512, respectively)	26,722	18,794	17,309
\$1,250, and \$1,086, respectively)	12,720	6,999	7,610
Total operating expenses	39,442	25,793	24,919
Loss from operations	(38,297)	(20,886)	(22,852)
Interest income, net	349	37	87
Net loss	\$(37,948)	\$(20,849)	\$(22,765)
Net loss per common share, basic and diluted	<u>\$ (0.44)</u>	<u>\$ (0.38)</u>	\$ (0.44)
Weighted average common shares outstanding, basic and diluted	<u>85,715</u>	55,116	52,183

The accompanying notes are an integral part of these consolidated financial statements.

### ACADIA PHARMACEUTICALS INC.

# CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS (in thousands)

	Years Ended December 31,		
	2013	2012	2011
Net loss	\$(37,948)	\$(20,849)	\$(22,765)
Other comprehensive loss:			
Unrealized gain (loss) on investment securities	45	(4)	9
Foreign currency translation adjustments	(1)	(1)	(512)
Comprehensive loss	\$(37,904)	\$(20,854)	\$(23,268)

The accompanying notes are an integral part of these consolidated financial statements.

## CONSOLIDATED STATEMENTS OF CASH FLOWS (in thousands)

	Years E	er 31,	
	2013	2012	2011
Cash flows from operating activities			
Net loss	\$ (37,948)	\$(20,849)	\$(22,765)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation	5,711	1,930	1,598
Amortization of premiums on investment securities	1,528	(133)	105
Depreciation and amortization	79	109	285
Non-cash charge resulting from lease termination	_	_	806
Gain on sales of property and equipment	(10)	(252)	_
Changes in operating assets and liabilities:			
Prepaid expenses, receivables and other current assets	(1,989)	320	(131)
Other assets	(179)	14	106
Accounts payable	(1,003)	(585)	(29)
Accrued expenses	2,413	635	277
Deferred revenue	(379)	(2,822)	(57)
Long-term liabilities	8		(92)
Net cash used in operating activities	(31,769)	(21,633)	(19,897)
Cash flows from investing activities			
Purchases of investment securities	(211,585)	(56,728)	(48,066)
Maturities of investment securities	86,087	30,948	54,049
Purchases of property and equipment	(618)	_	(3)
Proceeds from sales of property and equipment	12	252	
Net cash (used in) provided by investing activities	(126,104)	(25,528)	5,980
Cash flows from financing activities			
Proceeds from issuances of equity securities, net of issuance costs	111,682	98,204	14,022
Repayments of long-term debt		(32)	(78)
Net cash provided by financing activities	111,682	98,172	13,944
Effect of exchange rate changes on cash	(1)	(1)	13
Net (decrease) increase in cash and cash equivalents	(46,192)	51,010	40
Cash and cash equivalents			
Beginning of year	57,899	6,889	6,849
End of year	\$ 11,707	\$ 57,899	\$ 6,889
Supplemental schedule of noncash investing activities			
Unrealized gain (loss) on investment securities	\$ 45	\$ (4)	\$ 9
		. ,	

The accompanying notes are an integral part of these consolidated financial statements.

# CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (in thousands, except share data)

	Common Stock				Additional Paid-in	Accumulated	Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Capital	Deficit	Income (Loss)	Equity		
Balances at December 31, 2010	39,350,561	\$ 4	\$353,278	\$(324,106)	\$ 512	\$ 29,688		
Issuance of common stock and warrants, net of issuance costs  Issuance of common stock from exercise	12,565,446	1	13,899	_	_	13,900		
of stock options	10,434	_	13	_	_	13		
employee stock purchase plan	189,879	_	109	_	_	109		
with lease termination	782,339 —	_	1,322	(22,765)	_	1,322 (22,765)		
Stock-based compensation Other comprehensive loss	_	_	1,598	_	(503)	1,598 (503)		
Balances at December 31, 2011 Issuance of common stock and warrants,	52,898,659	\$ 5	\$370,219	\$(346,871)	\$ 9	\$ 23,362		
	19,000,000	2	80,536	_	_	80,538		
of stock options	293,595	_	453	_	_	453		
employee stock purchase plan	205,862	_	123	_	_	123		
of warrants on a net issuance basis Issuance of common stock under ATM	936,100	_	_	_	_	_		
Agreement, net of issuance costs Reclassification to redeemable common	5,347,137	1	17,089	_	_	17,090		
stock	(5,347,137)	(1) —	(17,657)	(20,849)	_	(17,658) (20,849)		
Stock-based compensation Other comprehensive loss		_	1,930	_	— (5)	1,930 (5)		
Balances at December 31, 2012	73,334,216	\$ 7	\$452,693	\$(367,720)	\$ 4	\$ 84,984		
Issuance of common stock in public offering, net of issuance costs	9,200,000	1	107,882	_	_	107,883		
of stock options	1,455,406	_	3,441	_	_	3,441		
employee stock purchase plan	122,853	_	358	_	_	358		
of warrants on a net issuance basis Reclassification from redeemable	1,643,006	_	_	_	_	_		
common stock	5,347,137	1 —	17,657	(37,948)	_	17,658 (37,948)		
Stock-based compensation Other comprehensive income	_	_	5,711		<u> </u>	5,711 44		
Balances at December 31, 2013	91,102,618	\$ 9	\$587,742	\$(405,668)	\$ 48	\$182,131		

The accompanying notes are an integral part of these consolidated financial statements.

#### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

#### 1. Organization and Nature of Operations

ACADIA Pharmaceuticals Inc. (the "Company") was originally incorporated in Vermont in 1993 as Receptor Technologies, Inc. The Company reincorporated in Delaware in 1997 and its operations are based in San Diego, California. The Company is focused on the development and commercialization of innovative small molecule drugs that address unmet medical needs in neurological and related central nervous system disorders.

The Company has incurred substantial operating losses since its inception due in large part to expenditures for its research and development activities. As of December 31, 2013, the Company had an accumulated deficit of \$405.7 million. The Company expects to continue to incur operating losses for at least the next several years as it pursues the development and commercialization of its product candidates.

The Company will require significant additional financing in the future to fund its operations. Future capital requirements will depend on many factors, including the progress in, the outcome of and the costs of the Company's development and regulatory activities, costs associated with establishing necessary sales and marketing capabilities, the scope, prioritization and number of its research and development programs, the ability of its collaborators and the Company to reach milestones and other events or developments under its collaboration and license agreements, and the ability of the Company to enter into new, and to maintain existing, collaboration and license agreements. Until the Company can generate significant continuing revenues, it expects to fund its operations through its existing cash, cash equivalents and investment securities, payments from existing and potential future collaborations, proceeds from public or private sales of its equity securities, debt financing, grant funding, or by licensing all or a portion of its product candidates or technology. The Company cannot be certain that adequate additional funding will be available on acceptable terms, or at all. Conditions in the financial markets and other factors could have a material adverse effect on the Company's ability to access sufficient funding on acceptable terms, or at all. If the Company cannot raise adequate additional capital, it will be required to delay, further reduce the scope of, or eliminate one or more of its research or development programs or its commercialization efforts. In such circumstances, the Company may also be required to relinquish greater, or even all, rights to product candidates at earlier stages of development or on less favorable terms than it would otherwise choose.

## 2. Summary of Significant Accounting Policies

Significant accounting policies followed in the preparation of these financial statements are as follows:

#### Principles of Consolidation

The accompanying consolidated financial statements include the accounts of the Company and its wholly owned subsidiary located in Europe. All intercompany accounts and transactions have been eliminated in consolidation.

## Cash and Cash Equivalents

The Company considers all highly liquid investments with an initial maturity date at the date of purchase of three months or less to be cash equivalents.

## **Investment Securities**

Investment securities are considered to be available-for-sale and are carried at fair value. Unrealized gains and losses, if any, are reported as a separate component of stockholders' equity. The cost of investment securities classified as available-for-sale is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion are included in interest income. Realized gains and losses, if any, are also included in interest income. The cost of securities sold is based on the specific identification method.

#### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

#### Fair Value of Financial Instruments

For financial instruments, consisting of cash and cash equivalents, accounts payable and accrued expenses included in the Company's financial statements, the carrying amounts are reasonable estimates of fair value due to their short maturities. Estimated fair values for investment securities, which are separately disclosed elsewhere, are based on quoted market prices for the instruments or other observable inputs.

## **Property and Equipment**

Property and equipment are recorded at cost and depreciated over their estimated useful lives (generally three to ten years) using the straight line method. Leasehold improvements are amortized over the shorter of their estimated useful lives or the term of the lease by use of the straight line method. Maintenance and repair costs are expensed as incurred. When assets are retired or sold, the assets and accumulated depreciation are removed from the respective accounts and any gain or loss is recognized.

#### Revenues

The Company recognizes revenues in accordance with authoritative guidance established by U.S. generally accepted accounting principles ("GAAP"). The Company's revenues are primarily related to its collaboration agreements, which may provide for various types of payments, including upfront payments, funding of research and development, milestone payments, and licensing fees. The Company's collaboration agreements also include potential payments for product royalties; however, the Company has not received any product royalties to date.

The Company considers a variety of factors in determining the appropriate method of accounting under its collaboration agreements, including whether the various elements can be separated and accounted for individually as separate units of accounting. Where there are multiple deliverables identified within a collaboration agreement that are combined into a single unit of accounting, revenues are deferred and recognized over the expected period of performance. The specific methodology for the recognition of the revenue is determined on a case-by-case basis according to the facts and circumstances of the applicable agreement.

Upfront, non-refundable payments that do not have stand-alone value are recorded as deferred revenue once received and recognized as revenues over the expected period of performance. Revenues from non-refundable license fees are recognized upon receipt of the payment if the license has stand-alone value, the Company does not have ongoing involvement or obligations, and the Company can determine the best estimate of the selling price for any undelivered items. When non-refundable license fees do not meet all of these criteria, the license revenues are recognized over the expected period of performance. Non-refundable payments for research funding are generally recognized as revenues over the period the related research activities are performed. Payments for reimbursement of external development costs are generally recognized as revenues using a contingency-adjusted performance model over the expected period of performance. Payments received from grants are recognized as revenues as the related research and development is performed and when collectability has been reasonably assured.

The Company evaluates milestone payments on an individual basis and recognizes revenues from non-refundable milestone payments when the earnings process is complete and collectability is reasonably assured. Non-refundable milestone payments related to arrangements under which the Company has continuing performance obligations are recognized as revenues upon achievement of the associated milestone, provided that (i) the milestone event is substantive and its achievability was not reasonably assured at the inception of the agreement and (ii) the amount of the milestone payment is reasonable in relation to the effort expended or the risk associated with the milestone event. Where separate milestone payments do not meet these criteria, the Company recognizes revenue using a contingency-adjusted performance model over the expected period of performance.

#### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

#### Research and Development Expenses

Research and development expenses are charged to operations as incurred. Research and development expenses include, among other things, costs associated with services provided by contract organizations for preclinical development, manufacturing of product candidates, and clinical trials. The Company accrues for costs incurred as the services are being provided by monitoring the status of the trial or services provided and the invoices received from its external service providers. In the case of clinical trials, a portion of the estimated cost normally relates to the projected cost to treat a patient in the trials, and this cost is recognized based on the number of patients enrolled in the trial. Other indirect costs are generally recognized on a straight-line basis over the estimated period of the study. As actual costs become known, the Company adjusts its accruals. Certain research and development programs are funded under agreements with collaboration partners, and the Company's costs related to these activities are included in research and development expenses.

#### Concentrations of Risk

Financial instruments, which potentially subject the Company to concentrations of credit risk, principally consist of cash, cash equivalents, and investment securities. The Company currently invests its excess cash primarily in a money market fund, U.S. Treasury notes, and high quality, marketable debt instruments of corporations, financial institutions and government sponsored enterprises. The Company has adopted an investment policy that includes guidelines relative to credit quality, diversification and maturities to preserve principal and liquidity.

During the years ended December 31, 2013, 2012 and 2011, revenues from the Company's agreements with certain collaborative partners exceeded 10 percent of its total revenues. During the year ended December 31, 2013, revenues from Allergan, Inc., the National Institutes of Health, and The Michael J. Fox Foundation comprised 50 percent, 19 percent, and 15 percent of total revenues, respectively. During the year ended December 31, 2012, revenues from Allergan and Meiji Seika Pharma Co., Ltd. ("Meiji Seika Pharma") comprised 23 percent and 66 percent of total revenues, respectively. During the year ended December 31, 2011, revenues from Allergan, Meiji Seika Pharma and The Michael J. Fox Foundation comprised 52 percent, 25 percent and 13 percent of total revenues, respectively.

#### Stock-Based Compensation

The fair value of each employee stock option and each employee stock purchase right granted is estimated on the grant date under the fair value method using the Black-Scholes model. The estimated fair value of each stock option and purchase right, including the effect of estimated forfeitures, is then expensed over the vesting period. The following assumptions were used to estimate the fair value of employee stock options:

	Years Ended December 31,		
	2013	2012	2011
Expected volatility	94%	98-99%	98%
Risk-free interest rate	1-2%	1%	1-2%
Expected forfeiture rate	8%	9%	10%
Expected dividend yield	0%	0%	0%
Expected life of options in years	6.0	5.8-6.0	5.8

*Expected Volatility.* The Company considers its historical volatility and implied volatility when determining the expected volatility.

#### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

*Risk-Free Interest Rate.* The risk-free interest rate is based on the implied yield currently available on U.S. Treasury zero-coupon issues with a remaining term approximating the expected term of the option.

Expected Forfeiture Rate. The Company considers its pre-vesting forfeiture history to determine its expected forfeiture rate.

Expected Dividend Yield. The Company has never paid any dividends and currently has no plans to do so.

Expected Life of Options. The Company considers, among other factors, its historical exercise experience to date as well as the mean time remaining to full vesting of all outstanding options and the mean time remaining to the end of the contractual term of all outstanding options.

The following assumptions were used to estimate the fair value of the purchase rights of each offering under the employee stock purchase plan that commenced during the indicated year:

	Years Ended December 31,		
	2013	2012	2011
Expected volatility	69-118%	69-137%	64-111%
Risk-free interest rate	0.1-0.3%	0.1-0.3%	0.1-0.4%
Expected dividend yield	0%	0%	0%
Expected life of offering in years	0.5 - 2.0	0.5-2.0	0.5-2.0

#### Income Taxes

Current income tax expense or benefit represents the amount of income taxes expected to be payable or refundable for the current year. A deferred income tax asset or liability is computed for the expected future impact of differences between the financial reporting and income tax bases of assets and liabilities and for the expected future tax benefit to be derived from tax credits and loss carryforwards. Deferred income tax expense or benefit represents the net change during the year in the deferred income tax asset or liability. Deferred tax assets are reduced by a valuation allowance when, in the opinion of management, it is more likely than not that some portion or all of the deferred tax assets will not be realized.

#### Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from these estimates.

## Long-Lived Assets

The Company assesses potential impairments to its long-lived assets when there is evidence that events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. An impairment loss is recognized when the estimated undiscounted cash flows expected to result from the use of the asset and its eventual disposition is less than its carrying amount. The amount of the impairment loss, if any, will generally be measured as the difference between the net book value of the assets and their estimated fair values. No such impairment losses have been recorded by the Company.

#### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

#### Comprehensive Income (Loss)

All components of comprehensive income (loss), including net income (loss), are reported in the financial statements in the period in which they are recognized. Comprehensive income (loss) is defined as the change in equity (net assets) of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. In accordance with accounting guidance, the Company presents the impact of any fluctuations in its foreign currency translation adjustments and any unrealized gains or losses on its investment securities in a separate statement of comprehensive income (loss) for each period.

#### Net Income (Loss) Per Common Share

Basic earnings (loss) per common share is computed by dividing net income (loss) by the weighted average number of common shares outstanding for the period. Diluted earnings (loss) per common share is computed by dividing net income (loss) by the weighted average number of common shares outstanding during the period, increased to include potential dilutive common shares that were outstanding during the period. The effect of outstanding stock options and warrants is reflected, when dilutive, in diluted earnings per common share by application of the treasury stock method. The Company has excluded all outstanding stock options and warrants from the calculation of diluted net loss per common share for the years ended December 31, 2013, 2012 and 2011 because all such securities were antidilutive. Shares used in calculating basic and diluted net loss per common share exclude these potential common shares:

	Years Ended December 31,		
	2013	2011	
	(i	n thousands	) —
Antidilutive options to purchase common stock	7,245	6,868	5,414
Antidilutive warrants to purchase common stock	3,116	4,388	4,559
	10,361	11,256	9,973

### Segment Reporting

Management has determined that the Company operates in one business segment. All revenues for the years ended December 31, 2013, 2012 and 2011 were generated in the United States.

#### Recently Issued Accounting Standards

In July 2013, the FASB issued authoritative guidance regarding the presentation of unrecognized tax benefits when a net operating loss carryforward exists. This authoritative guidance amends current guidance. The amended guidance clarifies that an unrecognized tax benefit, or a portion of an unrecognized tax benefit, should be presented in the financial statements as a reduction to a deferred tax asset for a net operating loss carryforward, a similar tax loss, or a tax credit carryforward if such settlement is required or expected in the event the uncertain tax position is disallowed. In situations where a net operating loss carryforward, a similar tax loss, or a tax credit carryforward is not available at the reporting date under the tax law of the applicable jurisdiction or the tax law of the jurisdiction does not require, and the entity does not intend to use, the deferred tax asset for such purpose, the unrecognized tax benefit should be presented in the financial statements as a liability and should not be combined with deferred tax assets. This amended guidance is effective prospectively for fiscal years, and interim periods within those years, beginning after December 15, 2013. The Company is evaluating the impact, if any, this guidance will have on its consolidated financial statements.

#### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

#### 3. Investment Securities

Investment securities included investment securities available-for-sale and, at December 31, 2012, investment securities classified as cash equivalents. Investment securities consisted of the following:

	December 31, 2013			
	Amortized Cost	Unrealized Gains	Unrealized (Losses)	Estimated Fair Value
		(in thou	usands)	
U.S. Treasury notes	\$ 2,743	\$ 4	\$	\$ 2,747
Government sponsored enterprise securities	78,537	28	(5)	78,560
Corporate debt securities	65,290	1	(9)	65,282
Commercial paper	27,468	_26		27,494
	\$174,038	\$59 ===	\$ (14)	\$174,083
		December	r 31, 2012	
	Amortized Cost	Unrealized Gains	Unrealized (Losses)	Estimated Fair Value
		(in thou	usands)	
U.S. Treasury notes	\$ 2,029	\$ 1	\$	\$ 2,030
Government sponsored enterprise securities	54,353	4	(5)	54,352
	\$ 56,382	<u>\$ 5</u>	<u>\$ (5)</u>	\$ 56,382

The Company has classified all of its investments securities available-for-sale, including those with maturities beyond one year, as current assets on the consolidated balance sheets based on the highly liquid nature of the investment securities and because these investment securities are considered available for use in current operations. As of December 31, 2013 and 2012, the Company held \$33.5 million and \$14.2 million, respectively, of available-for-sale investment securities with contractual maturity dates more than one year and less than two years.

#### 4. Fair Value Measurements

As of December 31, 2013, the Company held \$185.8 million of cash equivalents and available-for-sale investment securities consisting of a money market fund, U.S. Treasury notes, and high quality, marketable debt instruments of corporations, financial institutions and government sponsored enterprises. The Company has adopted an investment policy and established guidelines relating to credit quality, diversification and maturities of its investments to preserve principal and maintain liquidity. All investment securities have a credit rating of at least A3/A- or better, or P-1/A-1 or better, as determined by Moody's Investors Service or Standard & Poor's.

The Company's cash equivalents and available-for-sale investment securities are classified within the fair value hierarchy as defined by authoritative guidance. The Company's investment securities classified as Level 1 are valued using quoted market prices and the Company's investment securities classified as Level 2 are valued using other observable inputs such as recent trades for the securities or similar securities, interest rates on similar securities, or yield curves or benchmark interest rates observable at commonly quoted intervals. The Company does not hold any securities classified as Level 3, which are securities valued using unobservable inputs. The Company has not transferred any investment securities between the classifications. No other-than-temporary impairments were identified for the investment securities held by the Company as of December 31, 2013 or December 31, 2012.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

The fair value measurements of the Company's cash equivalents and available-for-sale investment securities are identified in the following tables (in thousands):

Fair Value Measurements at

		Reporting Date Using				
	December 31, 2013	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)		
Money market fund	\$ 11,748	\$11,748	\$ —	\$		
U.S. Treasury notes	2,747	2,747	_	_		
Government sponsored enterprise securities	78,560	_	78,560	_		
Corporate debt securities	65,282		65,282	_		
Commercial paper	27,494		27,494			
	\$185,831	<u>\$14,495</u>	<u>\$171,336</u>	<u>\$—</u>		

			alue Measuren porting Date Us	
	December 31, 2012	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market fund	\$ 51,216	\$51,216	\$ —	\$
U.S. Treasury notes	2,030	2,030	_	
Government sponsored enterprise securities	54,352		54,352	
	\$107,598	\$53,246	\$ 54,352	<u>\$—</u>

## **5. Balance Sheet Components**

Property and equipment, net, consisted of the following:

	Estimated Useful Lives	Decen	nber 31,
	(Years)	2013	2012
		(in the	ousands)
Machinery and equipment	5–7	\$ 875	\$ 2,578
Computers and software	3	863	981
Leasehold improvements	3-10	570	1,057
Furniture and fixtures	3-10	245	159
		2,553	4,775
Accumulated depreciation and amortization		(1,974)	(4,733)
		\$ 579	\$ 42

Depreciation and amortization of property and equipment was \$79,000, \$109,000, and \$285,000 for the years ended December 31, 2013, 2012, and 2011, respectively. During 2013, the Company retired \$2.8 million of fully depreciated property and equipment. During 2012, the Company sold \$1.5 million of fully depreciated machinery and equipment for a gain of \$252,000.

#### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

Accrued expenses consisted of the following:

	December 31,	
	2013	2012
	(in tho	usands)
Accrued research and development services	\$4,207	\$3,216
Accrued compensation and benefits	1,865	413
Accrued professional fees	308	364
Other	172	146
	\$6,552	\$4,139

### 6. Collaborative Research and Licensing Agreements

The Company has been a party to three collaboration agreements with Allergan. The March 2003 collaboration originally provided for a three-year research term, which was extended by the parties through March 2013. Pursuant to this agreement, the Company received an aggregate of \$19.5 million in payments, consisting of an upfront payment, research funding and related fees, through the conclusion of the collaboration in March 2013. The Company's two ongoing collaboration agreements with Allergan involve the development of product candidates in the areas of glaucoma and chronic pain. Under the glaucoma collaboration, the Company had received an aggregate of \$9.9 million in payments as of December 31, 2013, and is eligible to receive up to an aggregate of approximately \$15 million in additional payments per product upon the achievement of development and regulatory milestones. Under the chronic pain collaboration, the Company had received an aggregate of \$10.5 million in payments as of December 31, 2013, and is eligible to receive up to an aggregate of \$10 million in additional payments upon the achievement of development and regulatory milestones. The Company also is eligible to receive royalties on future product sales worldwide, if any, under each of the two ongoing collaboration agreements with Allergan. The Company recognized revenues, consisting of research funding, milestone and related fees, from its collaboration agreements with Allergan of \$571,000, \$1.1 million and \$1.1 million during each of the years ended December 31, 2013, 2012, and 2011.

In March 2009, the Company entered into a collaboration agreement with Meiji Seika Pharma. In July 2012, the Company and Meiji Seika Pharma jointly decided to discontinue the development program that was being pursued under the collaboration, and the collaboration agreement was terminated pursuant to its terms. Under the collaboration agreement, the Company had received \$3 million in non-refundable license fees as well as payments for the reimbursement of development costs that it had incurred during the collaboration. Payments received from Meiji Seika Pharma were deferred and recognized as revenues using a contingency-adjusted performance model over the estimated period of the Company's performance. Upon the termination of this collaboration agreement and the end of the Company's related performance obligations, the Company recognized as revenue the remaining deferred revenue from this collaboration during the third quarter of 2012. The Company recognized revenues relating to this collaboration of \$3.2 million and \$505,000 during the years ended December 31, 2012 and 2011, respectively.

Effective January 1, 2011, the Company prospectively adopted authoritative guidance for any new, or materially modified, multiple deliverable arrangement after the date of adoption. The Company has not entered into any new, or materially modified any, multiple deliverable arrangements since January 1, 2011. Accordingly, the collaborative agreements discussed above in this note that contain multiple deliverables continue to be accounted for under previously issued revenue recognition guidance for multiple deliverable arrangements. Under this prior guidance, the Company recognizes revenue for non-refundable payments upon receipt of the payment if the deliverable has stand-alone value, the Company does not have ongoing involvement or

#### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

obligations, and the fair value of any undelivered items can be determined. When non-refundable payments for deliverables do not meet all of these criteria, the payment is deferred and revenues are recognized over the expected period of performance. For a discussion of the Company's revenue recognition policy that would apply to any future multiple deliverable arrangement, see Note 2—Summary of Significant Accounting Policies—Revenues.

## 7. Stockholders' Equity

#### Public Offering

In May 2013, the Company raised net proceeds of \$107.9 million from the sale of 9,200,000 shares of its common stock in a public offering, including 1,200,000 shares sold pursuant to the exercise in full of the underwriters' over-allotment option.

#### Private Equity Financings

In December 2012, the Company raised net proceeds of \$80.5 million through the sale of 19,000,000 shares of its common stock at a price of \$4.43 per share and the sale of warrants to purchase 500,000 shares of its common stock at a price of \$4.42 per warrant share in a private equity financing. The warrants have an exercise price of \$0.01 per share and will expire on December 17, 2019. In accordance with authoritative accounting guidance, the warrants' value of \$2.2 million was determined on the date of grant using the Black-Scholes model with the following assumptions: risk free interest rate of 1.1 percent, volatility of 105.8 percent, a 7.0 year term and no dividend yield. These warrants were recorded as a component of stockholders' equity within additional paid-in capital. Per their terms, the outstanding warrants to purchase 500,000 shares of common stock may not be exercised if the holder's ownership of the Company's common stock would exceed 19.99 percent following such exercise. Pursuant to the terms of the private financing, the Company has an effective resale registration statement on file with the SEC covering shares of common stock sold and shares of common stock issuable upon the exercise of the warrants.

In January 2011, the Company raised net proceeds of \$13.9 million through the sale of 12,565,446 units at a price of \$1.19375 per unit in a private equity financing. Each unit consisted of one share of the Company's common stock and a warrant to purchase 0.35 shares of common stock. The warrants have an exercise price of \$1.38 per share and will expire on January 11, 2018. In accordance with authoritative accounting guidance, the warrants' value of \$3.3 million was determined on the date of grant using the Black-Scholes model with the following assumptions: risk free interest rate of 2.8 percent, volatility of 99.0 percent, a 7.0 year term and no dividend yield. These warrants were recorded as a component of stockholders' equity with an equal offsetting amount to stockholders' equity because the value of the warrants was considered a financing cost. During the year ended December 31, 2013, warrants to purchase 1,759,162 shares of common stock were exercised on a net issuance basis, resulting in the issuance of 1,643,006 shares of common stock. During the year ended December 31, 2012, warrants to purchase 1,172,774 shares of common stock were exercised on a net issuance basis, resulting in the issuance of 874,719 shares of common stock. At December 31, 2013, warrants to purchase 1,465,968 shares of common stock remained outstanding. Pursuant to the terms of the private financing, the Company has an effective resale registration statement on file with the SEC covering shares of common stock sold and shares of common stock issuable upon the exercise of the warrants.

#### Other Financing Transactions

In March 2012, the Company entered into an At-The-Market Issuance Sales Agreement ("ATM Agreement") with MLV & Co. LLC. During the year ended December 31, 2012, the Company raised gross proceeds of \$17.7 million from the sale of 5,347,137 shares of common stock under the ATM Agreement,

#### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

resulting in net proceeds of \$17.1 million after issuance costs. In November 2012, the Company determined that it had failed to timely file a Current Report on Form 8-K to report the election of a new director in January 2012. As a result, the Company was ineligible to use its effective shelf registration statement on Form S-3. Therefore, sales of the Company's common stock made pursuant to the ATM Agreement in 2012 and issued under the registration statement were subject to potential rescission rights that expired in 2013. No shareholder claimed or attempted to exercise any such rights. At December 31, 2012, the Company classified 5.3 million shares (\$17.7 million) of its common stock outside stockholders' equity because the potential redemption features were not within the control of the Company. These shares were treated as outstanding for financial reporting purposes.

#### Stock Option Plans

The Company's 2010 Equity Incentive Plan (the "2010 Plan") permits the grant of options to directors, officers, other employees, and consultants. In addition, the 2010 Plan permits the grant of stock bonuses, rights to purchase restricted stock, and other stock awards. The exercise price of options granted under the 2010 Plan cannot be less than 100 percent of the fair market value of the common stock on the date of grant and the maximum term of any option is ten years. Options granted under the 2010 Plan generally vest over a four-year period. All shares that remained eligible for grant under the Company's 2004 Equity Incentive Plan (the "2004 Plan") at the time of approval of the 2010 Plan were transferred to the 2010 Plan. The 2010 Plan share reserve also has been, and may be, increased by the number of shares that otherwise would have reverted to the 2004 Plan reserve after June 2010. At December 31, 2013, there were 14,048,237 shares of common stock authorized for issuance and 6,710,099 shares of common stock available for new grants under the 2010 Plan.

The 2004 Plan provided for the grant of options to directors, officers, other employees, and consultants. The exercise price of options granted under the 2004 Plan was at 100 percent of the fair market value of the common stock on the date of grant and the maximum term of any option was ten years. Options granted under the 2004 Plan generally vested over a four-year period. The Company's 1997 stock option plan (the "1997 Plan") provided for the grant of options to directors, officers, other employees, and consultants prior to the Company's initial public offering. The exercise price of each option grant was set at the fair market value for the Company's common stock as determined by the Company's Board of Directors and each option's maximum term was ten years. Options granted under the 1997 Plan generally vested over a four-year period.

Stock option transactions during the year ended December 31, 2013 are presented below:

	Number of Shares	Weighted- Average Exercise Prices	Weighted Average Remaining Contractual Term
Outstanding at January 1, 2013	6,948,456	\$ 3.08	
Granted	1,954,500	\$16.68	
Exercised	(1,455,406)	\$ 2.36	
Canceled/forfeited	(109,412)	\$ 5.04	
Outstanding at December 31, 2013	7,338,138	\$ 6.81	7.1
Vested and expected to vest at December 31, 2013	7,034,407	\$ 6.53	7.0
Exercisable at December 31, 2013	4,314,480	\$ 3.79	5.9

The aggregate intrinsic value of options outstanding and exercisable as of December 31, 2013, is calculated as the difference between the exercise price of the underlying options and the closing market price of the Company's common stock on that date, which was \$24.99. The aggregate intrinsic value of options outstanding

#### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

and exercisable as of December 31, 2013, was \$91.5 million. The aggregate intrinsic value of options exercised during the years ended December 31, 2013, 2012, and 2011 was approximately \$20.7 million, \$650,000, and \$6,000, respectively, determined as of the date of exercise. The Company received \$3.4 million in cash from options exercised during the year ended December 31, 2013.

The weighted average fair value of options granted during the years ended December 31, 2013, 2012, and 2011 was approximately \$12.66, \$1.51, and \$1.25, respectively. As of December 31, 2013, total unrecognized compensation cost related to stock options and purchase rights was approximately \$20.0 million, and the weighted average period over which this cost is expected to be recognized is 2.7 years.

The following table summarizes information about stock options outstanding at December 31, 2013:

	Options Outs	Options Exe	rcisable		
Range of Exercise Prices	Number of Shares	Weighted- Average Remaining Contractual Life	Weighted- Average Exercise Price	Number of Shares	Weighted- Average Exercise Price
\$0.96-\$ 1.56	1,589,996	6.9	\$1.42	1,405,676	\$1.43
\$1.57-\$ 1.86	1,273,411	7.3	\$1.65	913,487	\$1.66
\$1.87-\$ 2.39	1,443,343	7.3	\$2.14	842,284	\$2.11
\$2.40-\$14.89	1,275,608	4.3	\$8.09	971,503	\$8.45
\$14.90-\$27.47	1,755,780	9.0	\$18.36	181,530	\$15.61
	7,338,138		\$6.81	4,314,480	\$3.79

Stock-based awards issued to non-employees other than directors are accounted for using a fair value method and are re-measured to fair value at each period end until the earlier of the date that performance by the non-employee is complete or a performance commitment has been obtained. The fair value of each award is estimated using the Black-Scholes option pricing model with the following assumptions for the year ended December 31, 2013: dividend yield of 0 percent; volatility of 93 to 95 percent; risk free interest rate of 2 to 3 percent and remaining contractual life of 7 to 10 years. The stock compensation expense related to the grant of stock options to non-employees was \$584,000 for the year ended December 31, 2013 and was not significant for each of the years ended December 31, 2012 and 2011.

## Employee Stock Purchase Plan

The Company's 2004 Employee Stock Purchase Plan (the "Purchase Plan") became effective upon the closing of the Company's initial public offering in June 2004. The Purchase Plan includes an "evergreen" provision providing that an additional number of shares may be added to the shares authorized for issuance on the date of each annual meeting of stockholders for a period of ten years, which began with the meeting in 2005. Through December 31, 2013, a total of 1,375,000 shares of common stock had been reserved for issuance under the Purchase Plan. At December 31, 2013, 333,400 shares of common stock remained available for issuance pursuant to the Purchase Plan. Eligible employees who elect to participate in an offering under the Purchase Plan may have up to 15 percent of their earnings withheld, subject to certain limitations, to purchase shares of common stock pursuant to the Purchase Plan. The price of common stock purchased under the Purchase Plan is equal to 85 percent of the lower of the fair market value of the common stock at the commencement date of each offering period or the relevant purchase date. During the years ended December 31, 2013, 2012, and 2011, a total of 122,853, 205,862, and 189,879 shares of common stock were issued under the Purchase Plan at average prices of \$2.92, \$0.60, and \$0.57, respectively. The weighted average fair value of purchase rights granted during the

#### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

years ended December 31, 2013, 2012, and 2011 was \$10.96, \$2.43, and \$0.67, respectively. During the years ended December 31, 2013, 2012, and 2011, the Company recorded cash received from the exercise of purchase rights of \$358,000, \$123,000, and \$109,000, respectively.

#### Common Stock Reserved for Future Issuance

At December 31, 2013, a total of 7,338,138 and 1,965,968 shares of common stock were reserved for issuance pursuant to outstanding stock options and warrants, respectively.

#### 8. 401(k) Plan

Effective January 1997, the Company established a deferred compensation plan (the "401(k) Plan") pursuant to Section 401(k) of the Internal Revenue Code of 1986, as amended (the "Code"), whereby substantially all employees are eligible to contribute up to 60 percent of their pretax earnings, not to exceed amounts allowed under the Code. The Company makes discretionary contributions to the 401(k) Plan equal to 100 percent of each employee's pretax contributions up to 5 percent of his or her eligible compensation, subject to limitations under the Code. The Company's total contributions to the 401(k) Plan were \$240,000, \$180,000, and \$156,000 for the years ended December 31, 2013, 2012 and 2011, respectively.

#### 9. Income Taxes

At December 31, 2013, the Company had both federal and state net operating loss ("NOL") carryforwards of approximately \$360.9 million and \$332.5 million, respectively. Utilization of the NOL and research and development ("R&D") credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations that have occurred or that could occur in the future, as required by Section 382 of the Code, as well as similar state and foreign provisions. These ownership changes may limit the amount of NOL and R&D credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an "ownership change" as defined by Section 382 of the Code results from a transaction or series of transactions over a three-year period resulting in an ownership change of more than 50 percentage points of the outstanding stock of a company by certain stockholders or public groups.

The Company completed a study to assess whether an ownership change, as defined by Section 382 of the Code, had occurred from the Company's formation through December 31, 2013. Based upon this study, the Company determined that several ownership changes had occurred. Accordingly, the Company has reduced its deferred tax assets related to the federal and state NOL carryforwards and the federal R&D credit carryforwards that are anticipated to expire unused as a result of these ownership changes. These tax attributes have been excluded from deferred tax assets with a corresponding reduction of the valuation allowance with no net effect on income tax expense or the effective tax rate. Future ownership changes may further limit the Company's ability to utilize its remaining tax attributes.

Federal and state NOL carryforwards of \$3.6 million and \$7.5 million will expire in 2018 and 2014, respectively, unless utilized. The remaining federal and state NOL carryforwards will begin to expire in 2019 and 2015, respectively. At December 31, 2013, the Company had \$8.0 million of federal R&D credit carryforwards of which \$119,000 will expire in 2018 unless utilized, and the remaining federal R&D credit carryforwards will begin to expire in 2019. At December 31, 2013, the Company had \$4.9 million of state R&D credit carryforwards that have no expiration date. At December 31, 2013, the Company also had foreign NOL carryforwards of approximately \$4.1 million that have no expiration date. The Company continues to record the deferred tax assets related to these attributes, subject to valuation allowance, until expiration occurs.

#### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

Approximately \$16.4 million of the NOL carryforwards relate to excess tax deductions for stock compensation, the income tax benefit of which will be recorded as additional paid-in capital if and when realized.

The components of the deferred tax assets are as follows:

	2013	2012
	(in thousands)	
NOL carryforwards	\$ 136,583	\$ 127,894
R&D credit carryforwards	11,227	11,056
Capitalized R&D	8,003	4,075
Stock-based compensation	3,221	2,906
Other	1,207	775
	160,241	146,706
Valuation allowance	(160,241)	(146,706)
	<u>\$</u>	<u>\$</u>

Realization of deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Accordingly, the deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by \$13.5 million in 2013 primarily due to an increase in deferred tax assets generated from net operating losses and R&D credits, partially offset by the expiration of NOL carryforwards in 2013.

A reconciliation of income taxes to the amount computed by applying the statutory federal income tax rate to the net loss is summarized as follows:

2011		
(in thousands)		
88) \$(7,73	34)	
09 30	06	
	_	
37) (51	14)	
75 8,82	20	
71) (1,28	88)	
(4)	59	
16 36	68	
0 \$ 1	17	
a 20 20 3'	088) \$(7,72) 209 30  937) (5 375 8,82 171) (1,22) (4) 616 30	

The net income tax expense for each of the years ended December 31, 2013, 2012 and 2011 is recorded in the Company's statement of operations in general and administrative expenses.

The tax years 1998-2013 remain open to examination by the major taxing jurisdictions to which the Company is subject. During 2012, the Internal Revenue Service concluded an exam for tax years 2008 and 2009 that resulted in favorable adjustments to the Company's R&D credits. As of December 31, 2013 and 2012, the Company did not have any liabilities recorded for uncertain tax positions.

## 10. Commitments and Contingencies

The Company leases facilities and certain equipment under noncancelable operating leases that expire at various dates through December 2016. Under the terms of the facilities leases, the Company is required to pay its proportionate share of property taxes, insurance and normal maintenance costs.

#### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

Future noncancelable minimum payment obligations under operating lease arrangements were as follows at December 31, 2013:

Year Ending	(in th	ousands)
2014	\$	838
2015		866
2016		583
2017		_
Thereafter		
	\$	2,287

Rent expense was \$594,000, \$663,000, and \$2.1 million for the years ended December 31, 2013, 2012, and 2011, respectively. Facility operating leases contain escalation clauses. The Company recognizes rent expense on a straight line basis over the lease term. The difference between rent expense recorded and amounts paid under lease agreements is recorded as deferred rent.

In April 2011, the Company entered into a termination agreement related to the lease for its Swedish research facility and ceased operations at this site. The lease was entered into in June 2005 and had a 10-year term. Pursuant to this agreement, the Company made a one-time payment of \$690,000 and issued 782,339 shares of its common stock to the landlord in settlement of all lease-related obligations. General and administrative expenses for the year ended December 31, 2011 included a net charge of \$1.1 million, which amount consisted of \$1.7 million in lease termination charges, offset by a \$539,000 reduction in the Company's cumulative translation adjustment balance related to the liquidation of substantially all assets of its Swedish subsidiary.

The Company has entered into agreements with contract research organizations and other external service providers primarily for services in connection with the development of its product candidates. The Company was contractually obligated for up to approximately \$19.1 million of future services under these agreements as of December 31, 2013. The nature of the work being conducted under the Company's agreements with contract research organizations is such that, in most cases, the services may be stopped with short notice. In such event, the Company would not be liable for the full amount of the contract. The Company's actual contractual obligations may vary depending upon several factors, including the progress and results of the underlying studies.

In November 2006, the Company entered into an agreement with the Ipsen Group pursuant to which it licensed certain intellectual property rights that complement its patent portfolio for its serotonin platform, including pimavanserin. If certain conditions are met, the Company would be required to make future payments, including milestones, sublicensing fees and royalties. The amount of potential future milestones payments is \$10.5 million in the aggregate, which amount would be offset by any sublicensing fees the Company may pay under the agreement. Because these milestone payments would only be payable upon the achievement of specified regulatory events and it is uncertain when, or if, such events will occur, the Company cannot forecast with any degree of certainty when, or if, it will be required to make payments under the agreement.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

## 11. Selected Quarterly Financial Data (Unaudited)

2013	March 31,	June 30,	September 30,	December 31,
<del></del>	(in thousands, except per share data)			
Revenues	\$ 417	\$ 451	\$ 240	\$ 37
Net loss	\$(6,123)	\$(9,081)	\$(10,695)	\$(12,049)
Net loss per common share, basic and diluted	\$ (0.08)	\$ (0.11)	\$ (0.12)	\$ (0.13)
2012	March 31,	June 30,	September 30,	December 31,
	(in thousands, except per share data)			
Revenues	\$ 450	\$ 599	\$ 3,478	\$ 380
Net loss	\$(6,218)	\$(5,419)	\$ (2,402)	\$ (6,810)
Net loss per common share, basic and diluted	\$ (0.12)	\$ (0.10)	\$ (0.04)	\$ (0.11)

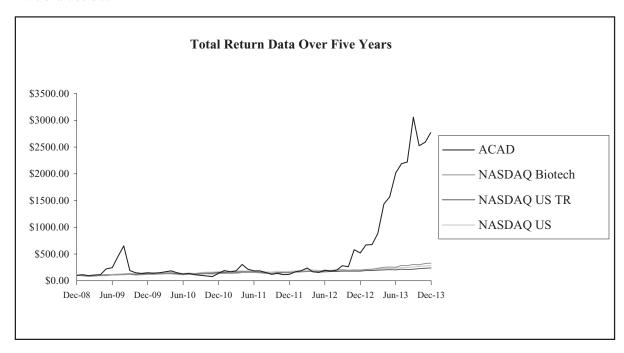
Revenues and net loss are rounded to thousands each quarter. Therefore, the sum of the quarterly amounts may not equal the annual amounts reported. Net loss per common share, basic and diluted, are computed independently for each quarter and the full year based upon respective average shares outstanding. Therefore, the sum of the quarterly net loss per common share amounts may not equal the annual amounts reported.

#### PERFORMANCE MEASUREMENT COMPARISON

The material in this section is not "soliciting material," is not deemed "filed" with the United States Securities and Exchange Commission, and is not to be incorporated into any filing of ACADIA Pharmaceuticals Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date hereof and irrespective of any general incorporation language contained in such filing.

The following graph shows a comparison of the total cumulative returns of an investment of \$100 in cash from December 31, 2008 through December 31, 2013 in (i) our common stock, (ii) the NASDAQ Biotechnology Index, (iii) the NASDAQ U.S. Benchmark TR Index, and (iv) the NASDAQ U.S. Stock Market Index. The comparisons in the graph are required by the SEC and are not intended to forecast or be indicative of the possible future performance of our common stock. The graph assumes that all dividends have been reinvested (to date, we have not declared any dividends).

Effective January 2014, NASDAQ OMX has replaced total return values prepared by the Center for Research in Security Prices with its own NASDAQ OMX Global Index data. As a result of this change, the NASDAQ U.S. Stock Market Index has been replaced with the NASDAQ U.S. Benchmark TR Index. Both indexes are reflected in the chart below.



## Corporate Information

#### **EXECUTIVE OFFICERS**

#### Uli Hacksell, Ph.D.

Chief Executive Officer and Director

#### Thomas H. Aasen\*

Executive Vice President, Chief Financial Officer and Chief Business Officer

#### Roger G. Mills, M.D.

Executive Vice President,
Development and Chief Medical Officer

#### Terrence O. Moore

Executive Vice President and Chief Commercial Officer

#### Glenn F. Baity

Vice President, General Counsel and Secretary

## **BOARD OF DIRECTORS**

#### Leslie L. Iversen, Ph.D.

Chairman of the Board Professor of Pharmacology University of Oxford, England

#### Stephen R. Biggar, M.D., Ph.D.

Partner

Baker Brothers Investments

#### Michael T. Borer

Former Chief Executive Officer and President, Xcel Pharmaceuticals, Inc.

#### Laura A. Brege

Chief Executive Officer and President Nodality, Inc.

## Mary Ann Gray, Ph.D.

President

Gray Strategic Advisors, LLC

#### Uli Hacksell, Ph.D.

Chief Executive Officer ACADIA Pharmaceuticals Inc.

#### Lester J. Kaplan, Ph.D.

Former Executive Vice President and President, Research and Development, Allergan, Inc.

#### Torsten Rasmussen

Chief Executive Officer and President Morgan Management ApS

## William (Bill) M. Wells

Founder and Chairman, Evizone Limited Former Chief Executive Officer Biovail Corporation

#### **CORPORATE HEADOUARTERS**

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#### COMMON STOCK LISTING

Ticker Symbol: ACAD, The NASDAQ Global Market

#### ANNUAL STOCKHOLDERS' MEETING

ACADIA Pharmaceuticals' Annual Stockholders' Meeting will be held on Friday, June 6, 2014, at the Hilton La Jolla Torrey Pines at 10950 N. Torrey Pines Road, La Jolla, CA 92037

#### STOCK TRANSFER AGENT AND REGISTRAR

Computershare Trust Company, N.A. 250 Royall St. Canton, MA 02021 Telephone: (800) 851-3061 www.computershare.com/us

#### **COMPANY COUNSEL**

Cooley LLP 4401 Eastgate Mall San Diego, CA 92121

#### INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

PricewaterhouseCoopers LLP 5375 Mira Sorrento Place, Suite 300 San Diego, CA 92121

## STOCKHOLDERS' INQUIRIES

Stockholders may obtain copies of our news releases, Securities and Exchange Commission filings, including Forms 10-K, 10-Q, and 8-K, and other company information by accessing our website at www.acadia-pharm.com. Stockholders may also contact Investor Relations at (858) 558-2871.

#### FORWARD-LOOKING STATEMENTS

Statements in this report that are not strictly historical in nature are forward-looking statements. These statements include but are not limited to statements related to the progress and timing of our drug development programs and related trials, the utility, safety, efficacy and benefits of our product candidates, the future development and commercialization of pimavanserin in a variety of indications, potential approval of pimavanserin, and future growth for ACADIA or its stockholders. These statements are only predictions representing ACADIA's expectations and beliefs as of the date this report was prepared based on then-current information. Actual events or results may differ materially from those projected in any of such statements due to various factors, including the risks and uncertainties inherent in drug discovery, development and commercialization, risks of regulatory approval, and the risk that past results of clinical trials may not be indicative of future trial results. For a discussion of these and other factors, please refer to ACADIA's Annual Report on Form 10-K for the year ended December 31, 2013, as well as other subsequent filings with the Securities and Exchange Commission. You are cautioned not to place undue reliance on these forward-looking statements. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. All forward-looking statements are qualified in their entirety by this cautionary statement and ACADIA undertakes no obligation to revise or update this report to reflect future events or circumstances after the date hereof, except as required by law.

<sup>\*</sup>Retired from ACADIA in April 2014.



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