ACADIA Pharmaceuticals

FORM 10-K AND PERFORMANCE MEASUREMENT GRAPH

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

Form 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2014

Or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from to

Commission File Number: 000-50768

ACADIA PHARMACEUTICALS INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**06-1376651**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification Number)**
11085 Torreyana Road, Suite 100 San Diego, California	**92121**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's telephone number, including area code:
(858) 558-2871

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

Title of each class	**Name of each exchange on which registered**
Common Stock, par value $0.0001 per share	**The NASDAQ Global Select Market**

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

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934. Yes ☐ No ☒

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See definitions of "large accelerated filer", "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Securities Exchange Act of 1934:

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

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Securities Exchange Act of 1934). Yes ☐ No ☒

As of June 30, 2014, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the registrant's common stock held by non-affiliates of the registrant was approximately $1.4 billion, based on the closing price of the registrant's common stock on the NASDAQ Global Select Market on June 30, 2014 of $22.59 per share.

As of January 30, 2015, 100,171,719 shares of the registrant's common stock, $0.0001 par value, were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement to be filed with the Securities and Exchange Commission by April 30, 2015 are incorporated by reference into Part III of this report.

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 and cause our results to differ materially from those expressed or implied by our forward-looking statements. 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 medicines that address unmet medical needs in neurological and related central nervous system disorders. Led by our novel drug candidate NUPLAZID™ (pimavanserin) for the treatment of Parkinson's disease psychosis, we have a portfolio of product opportunities including the following:

- ***Parkinson's disease psychosis (PDP).*** We have reported positive Phase III pivotal trial results in PDP and believe NUPLAZID has the potential to be the first drug approved in the United States for this disorder. We are currently completing a New Drug Application, or NDA, for NUPLAZID for the treatment of PDP and related preparations to support a review of the NDA by the U.S. Food and Drug Administration, or FDA. We plan to submit the NDA to the FDA in the first quarter of 2015. In 2014, we announced that the FDA has granted Breakthrough Therapy designation for NUPLAZID for the treatment of PDP.
- ***Alzheimer's disease psychosis (ADP).*** We are currently conducting a Phase II study exploring the utility of pimavanserin for the treatment of Alzheimer's disease psychosis, or ADP. No drug is currently approved by the FDA for the treatment of this disorder.
- ***Schizophrenia.*** We have successfully completed a Phase II study of pimavanserin in the treatment of schizophrenia where we observed significant anti-psychotic effects when pimavanserin was co-administered with a low dose of risperidone, a generic drug currently approved for the treatment of schizophrenia. We next plan to evaluate the use of pimavanserin as a stand-alone maintenance therapy between acute psychotic episodes in a Phase II schizophrenia study.

- ***Sleep disturbances.*** Pimavanserin has shown significant benefits in nighttime sleep and daytime wakefulness in studies conducted in elderly patients with PDP. In 2015, we plan to follow up these findings with a Phase II study to further explore the potential sleep benefits of pimavanserin in Parkinson's disease patients.

We hold worldwide commercialization rights to pimavanserin. Our pipeline also includes clinical-stage programs for chronic pain and glaucoma in collaboration with Allergan, Inc.

We were originally incorporated in Vermont in 1993 as Receptor Technologies, Inc. We reincorporated in Delaware in 1997 and our headquarters are in San Diego, California. 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.

We own or have rights to various trademarks, copyrights and tradenames used in our business, including ACADIA® and NUPLAZID™. 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 endorsement or sponsorship of us, by the trademark or trade dress owners.

Our Strategy

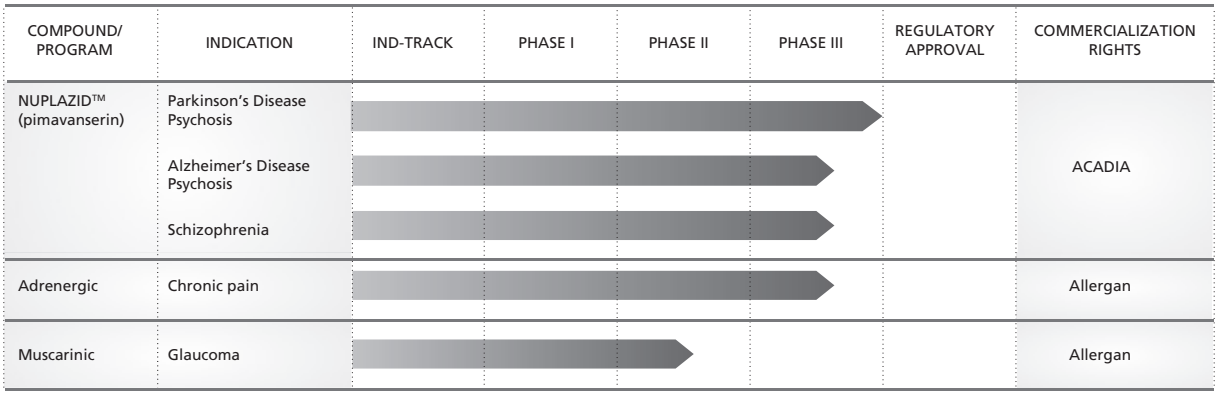
Our strategy is to discover, develop, and commercialize innovative small molecule drugs that address unmet medical needs in neurological and related central nervous system disorders. We have assembled a management team with significant industry experience to lead the discovery, development, and commercialization of our product opportunities. We complement our management team with scientific and clinical advisors, including recognized experts in the fields of Parkinson's disease psychosis, Alzheimer's disease psychosis, schizophrenia, and other central nervous system disorders. Key elements of our strategy are to:

- ***Develop and commercialize our lead product candidate, NUPLAZID, for Parkinson's disease psychosis.*** We are pursuing Parkinson's disease psychosis as our lead indication for NUPLAZID, for which we plan to submit an NDA to the FDA in the first quarter of 2015. If approved, NUPLAZID would be the first drug approved by the FDA for the treatment of Parkinson's disease psychosis. If approved, we intend to commercialize NUPLAZID for this indication in the United States by establishing a specialty sales force focused primarily on neurologists and a small group of psychiatrists and long-term care physicians who are high prescribers of antipsychotics for Parkinson's disease psychosis patients. Outside of the United States, we may choose to commercialize NUPLAZID in selected markets by establishing one or more strategic alliances.
- ***Leverage the commercial potential of pimavanserin by expanding to additional neurological and psychiatric disorders.*** We intend to pursue the development and commercialization of pimavanserin in 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 have also observed significant sleep benefits of pimavanserin in studies conducted in elderly patients with Parkinson's disease psychosis and plan to further explore these benefits in a Phase II study in Parkinson's disease patients. 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.

- ***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 may in-license or acquire assets, which could include clinical-stage product candidates or commercial-stage products, to leverage the sales force that we intend to establish.
- ***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. While our resources are currently focused on the development and commercialization of pimavanserin, we may 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 portfolio will mitigate risks inherent in drug development and increase the likelihood of our success.

Our Product Opportunities

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



NUPLAZID (Pimavanserin)

Pimavanserin is a new chemical entity that we discovered and that has successfully completed Phase III development, potentially positioning it to be the first drug approved in the United States for the treatment of Parkinson's disease psychosis. During 2014, the FDA provisionally accepted NUPLAZID as the trade name for pimavanserin. NUPLAZID (pimavanserin) selectively blocks the activity of the 5-HT_{2A} receptor, a key serotonin receptor that plays an important role in psychosis. We hold worldwide commercialization rights to NUPLAZID (pimavanserin) for all indications and have established a broad patent portfolio, which includes numerous issued patents in the United States, Europe, and several additional countries.

We are pursuing Parkinson's disease psychosis as our lead indication for NUPLAZID. We have completed a successful pivotal Phase III trial with NUPLAZID in patients with Parkinson's disease psychosis, the -020 Study. Following this study, we met with the FDA in 2013, and announced that the agency agreed that the data from the -020 Study, together with supportive data from our other studies with NUPLAZID, are sufficient to support the filing of an NDA for the treatment of Parkinson's disease psychosis. In 2014, the FDA granted Breakthrough Therapy designation for NUPLAZID for the treatment of Parkinson's disease psychosis. The Breakthrough Therapy designation was created by the FDA to expedite the development and review of drugs that are intended to treat serious or life-threatening conditions. If approved, we intend to commercialize NUPLAZID for Parkinson's disease psychosis in the United States by establishing a specialty sales force focused primarily on neurologists and a small group of psychiatrists and long-term care physicians who are high prescribers of antipsychotics for Parkinson's disease psychosis patients. Starting in the second half of 2013, we began to hire

the senior leadership of our commercial organization. Our preparations are underway for the planned future launch of NUPLAZID and we plan to hire a commercial sales force to coincide approximately with a NUPLAZID approval, if any. In addition to building our commercial capabilities, we are expanding our existing infrastructure to support the planned launch and commercialization of NUPLAZID, including adding to our commercial level manufacturing, medical affairs, quality control and compliance capabilities. As was the case with the -020 Study and our other clinical trials, if approved, NUPLAZID will be administered in two 17 mg tablets taken together once a day.

We believe that pimavanserin also has the potential to address other neurological and psychiatric disorders, including Alzheimer's disease psychosis and schizophrenia. We are currently conducting a Phase II study to examine the efficacy and safety of pimavanserin as a treatment for 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 of pimavanserin as a stand-alone maintenance therapy to treat schizophrenia between acute psychotic episodes.

NUPLAZID as a Treatment for Parkinson's Disease Psychosis

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 psychosis is a debilitating disorder commonly characterized by visual hallucinations and delusions that occurs in an estimated 40 percent of Parkinson's disease patients. 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.

The FDA has not approved any drug to treat Parkinson's disease psychosis. 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. These drugs 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-HT_{2A} 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.

NUPLAZID 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.

In November 2012, we announced successful top-line results from our pivotal Phase III -020 Study, evaluating the efficacy, tolerability, and safety of NUPLAZID 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 multi-center, 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 34 mg of NUPLAZID (the equivalent of 40mg of pimavanserin tartrate) 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.

NUPLAZID 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. NUPLAZID 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, NUPLAZID 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 NUPLAZID, are sufficient to support the filing of an NDA for the treatment of Parkinson's disease psychosis. In September 2014, we announced that the FDA has granted Breakthrough Therapy designation for NUPLAZID for the treatment of Parkinson's disease psychosis. The Breakthrough Therapy designation was created by the FDA to expedite the development and review of drugs that are intended to treat serious or life-threatening conditions.

We also are continuing to conduct our open-label safety extension study, 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 study from our earlier Phase II Parkinson's disease psychosis trial, has generated a considerable amount of long-term safety data on NUPLAZID. A total of over 250 patients have been treated with NUPLAZID for at least one year, and of those at least 100 patients have been treated for at least two years. Our longest single-patient exposure is greater than nine years. We believe that our experience to date suggests that long-term administration of NUPLAZID is generally safe and well tolerated in this elderly and fragile patient population.

During 2014, we conducted foundational access and reimbursement research with key decision makers for payers covering 168 million lives, of which approximately one-third are covered by commercial healthcare payers, one-third covered by Medicare Part D Standard, and one-third covered by Medicare Part D Low Income Subsidy.

While the FDA has agreed to review an NDA for NUPLAZID on the basis of our positive pivotal -020 Study data, along with supportive efficacy and safety data from other NUPLAZID studies, the NDA will be subject to 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

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. 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 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.

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 200 patients with Alzheimer's disease psychosis. Following a screening period that includes brief psycho-social therapy, patients are randomized on a one-to-one basis to receive either 34 mg of pimavanserin (the equivalent of 40mg of pimavanserin tartrate) or placebo once-daily for twelve weeks. The -019 study will assess several key efficacy endpoints, including use of the Neuropsychiatric Inventory—Nursing Home 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. We plan to complete enrollment in the -019 Study by the end of 2015.

Pimavanserin as a Treatment for 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. Antipsychotic 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.

Most schizophrenia patients in the United States today are treated with second-generation, or atypical, antipsychotics, which induce fewer motor disturbances than typical, or first-generation, 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-HT_{2A} 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.

Pimavanserin's selective blockade of the 5-HT_{2A} receptor may enable it to be used in two different treatment approaches to improve the therapy for patients with schizophrenia. First, we are planning to evaluate the use of pimavanserin between acute psychotic episodes in a Phase II schizophrenia study. In this maintenance phase of schizophrenia therapy, we believe that pimavanserin may be desirable to use as a treatment that selectively blocks the 5-HT_{2A} receptor and avoids interaction with dopamine receptors, which may be associated with many of the side effects caused by existing antipsychotic drugs. We believe that pimavanserin has 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.

Second, we believe that pimavanserin may be effective as a co-therapy, together with low doses of existing atypical antipsychotic drugs such as risperidone, to obtain a more optimal balance between 5-HT_{2A} 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. 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.

Sleep Benefits of Pimavanserin

Although Parkinson's disease is typically characterized by motor dysfunction, non-motor problems are also common and can significantly impair function and quality of life. In studies of Parkinson's disease patients, the prevalence of sleep disturbances, including daytime wakefulness, has been reported to be almost 100 percent. Sleep disorders are a major cause of disability in Parkinson's disease and are associated with other symptoms including falls, psychosis, dementia, and depression, which have a substantial impact on quality of life.

Sleep-related problems in Parkinson's disease can be divided into disturbances of nocturnal sleep and disturbances of daytime wakefulness. Studies suggest that nighttime sleep disturbances occur in almost 70 percent of Parkinson's disease patients. These disturbances include insomnia, restless legs syndrome, periodic leg movements of sleep, rapid eye movement sleep behavior disorder, and sleep apnea. Impaired nighttime sleep has been associated with increased daytime sleepiness, depression, fatigue, and cognitive impairment.

Clinical benefits of pimavanserin were observed in an exploratory efficacy measure of sleep during our -020 Study. Sleep was assessed using the SCOPA-sleep scale, which was designed to enable the investigator to evaluate nighttime sleep and daytime wakefulness in Parkinson's disease patients. Pimavanserin demonstrated significant improvements on both nighttime sleep ($p=0.045$) and daytime wakefulness ($p=0.012$) on SCOPA. We plan to follow up these findings with a Phase II study to further explore the potential sleep benefits of pimavanserin in Parkinson's disease patients.

Adrenergic and Muscarinic Programs

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. 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.

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. 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.

In November 2014, Allergan announced it entered into an agreement with Actavis plc under which Actavis will acquire Allergan. If this acquisition is completed, we do not know what impact, if any, it will have on our programs with Allergan or Allergan's performance thereunder.

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 are successful in developing pimavanserin and gaining FDA approval of NUPLAZID, it would compete with a variety of established drugs in the areas of Parkinson's disease psychosis, Alzheimer's disease psychosis, and schizophrenia. For example, NUPLAZID for the treatment of Parkinson's disease psychosis would compete with off-label use of antipsychotic drugs, including Seroquel, marketed by Astra-Zeneca PLC, and clozapine, a generic drug.

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

Our potential products for the treatment of chronic pain would compete with Lyrica, marketed by Pfizer Inc., 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, sales and marketing, 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 effect on our business.

Intellectual Property

We currently hold 49 issued U.S. patents and 244 issued foreign patents. All of these patents originated from discoveries made by us. In addition, we have 15 provisional and utility U.S. patent applications and 52 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. In connection with a successful filing of the NDA for NUPLAZID, we would pay a $2.5 million milestone payment to Ipsen and, if approved, would pay an additional $8.0 million milestone payment to Ipsen, each pursuant to the terms of

the 2006 license agreement. In addition, if we are able to successfully market and sell NUPLAZID, we would pay to Ipsen royalties of up to two percent of net product sales pursuant to the agreement. We are a party to various other license agreements that give us rights to use certain technologies in our research and development.

Pimavanserin

Twenty U.S. patents have been issued to us that provide protection for pimavanserin, including two that cover the compound generically and 12 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 56 issued foreign patents that specifically cover pimavanserin, including patents in 38 European countries, Australia, Canada, China, Hong Kong, India, Japan, Mexico, New Zealand, Russia, Singapore and South Africa, which provide patent protection until 2024. We also have 48 issued foreign patents that cover polymorphs of pimavanserin and provide patent protection until 2025. 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.

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, 2014, 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 $15.0 million in additional payments per product upon the achievement of development and regulatory milestones as well as royalties on future net 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, 2014 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 net 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.

In November 2014, Allergan announced it entered into an agreement with Actavis under which Actavis will acquire Allergan. If this acquisition is completed, we do not know what impact, if any, it will have on our agreements with Allergan or Allergan's performance thereunder.

Government Regulation

Our business activities, including 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, import, export, 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 recently enacted and any applicable future healthcare reform measures. In addition, we are subject to state and federal laws, including, among others, anti-kickback laws, false claims laws, data privacy and security laws, and transparency laws that restrict certain business practices in the pharmaceutical industry.

In the United States, drug product candidates intended for human use undergo laboratory and animal testing until adequate proof of safety is established. Clinical trials for new product candidates are then typically conducted in humans 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 an Investigational New Drug Application, or IND, to the FDA.

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 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, or GCPs. Additionally, the manufacture of our drug product, must be done in accordance with current good manufacturing practices, or GMPs.

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. 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 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 can choose to inspect the facilities at which the product is manufactured and will not approve the product unless the manufacturing facility complies with GMPs. The FDA may also audit sites at which clinical trials have been conducted to determine compliance with GCPs and data integrity. 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. The FDA is not bound by the recommendation of an advisory committee.

In addition, delays or rejections may be encountered based upon changes in regulatory policy, regulations or statutes governing product approval during the period of product development and regulatory agency review.

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 in 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 payment of significant annual fees and 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.

In addition, as a condition of approval, the FDA may require an applicant to develop a risk evaluation and mitigation strategy, or REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product.

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, which may result in delay or failure to approve applications, warning letters, product recalls and/or imposition of fines or penalties.

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

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 other transfers of value to healthcare professionals and entities.

Drugs for Serious or Life-Threatening Illnesses

In 2012, Congress enacted the Food and Drug Administration Safety and Innovation Act, or FDASIA. This law established a new regulatory scheme allowing for expedited review of products designated as "breakthrough therapies". A product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process, providing timely advice to the product sponsor regarding development and approval, involving more senior staff in the review process, assigning a cross-disciplinary project lead for the review team, and taking other steps to design the clinical trials in an efficient manner. FDA regulations also provide certain mechanisms to expedite 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. Under accelerated approval regulations, NDAs may be approved on the basis of valid surrogate markers of product effectiveness, thus accelerating the normal approval process. Certain of our product candidates might qualify for accelerated approval. Even if the FDA agrees that these potential products qualify for accelerated approval procedures or breakthrough therapy designation, 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 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 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 other 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 NUPLAZID, 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 Centers for Medicare and Medicaid Services, or CMS, recently proposed, but did not adopt, changes to this policy for coverage year 2015. If this policy is changed in the future and if CMS no longer considers the antipsychotic class to be of "critical concern", 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, among others, anti-kickback and false claims laws, data privacy and security laws, and transparency laws. 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 good, facility, 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 or even potentially beneficial in other industries. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions 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 Anti-Kickback Statute may have been violated, and enforcement will depend on the relevant facts and circumstances.

The federal False Claims Act prohibits any person or entity 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, for example, allegedly causing false claims to be submitted because of their marketing of products for unapproved, and thus non-reimbursable, uses.

Additionally, other federal and state false claims and false statements laws exist that restrict business activities in the pharmaceutical industry. 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. In addition, the federal civil monetary penalties statute imposes penalties against any person or entity that, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. 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.

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.

In addition, a federal requirement created under the ACA mandates that pharmaceutical companies track and annually 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. CMS disclosed certain reported information for the first reporting period on a publicly available website in September 2014. 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. 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 exceptions, 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 other 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, 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 payors 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 certain 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, which went into effect in April 2013 and will remain in effect through 2024 unless additional Congressional action is taken, 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.

Research and Development Expenses

Our research and development expenses were $60.6 million, $26.7 million, and $18.8 million in 2014, 2013, and 2012, respectively.

Manufacturing and Distribution

We currently outsource, and plan to continue to outsource, manufacturing responsibilities for our existing and future product candidates, including NUPLAZID, for development and commercial purposes. Until recently, NUPLAZID has been manufactured in small quantities for preclinical studies and clinical trials. If NUPLAZID is approved for commercial sale, we will need to manufacture the product in larger quantities. Significant scale-up of manufacturing requires additional process development and validation studies, which will be subject to FDA review as part of our NDA submission. Our active pharmaceutical ingredient, or API, has been manufactured in Switzerland for over ten years and we anticipate continuing to use this manufacturer as we transition to a commercial organization.

We plan to retain third-party service providers to perform a variety of functions related to the distribution of NUPLAZID, including warehousing, customer service, order-taking, invoicing, collections, and shipment and returns processing.

Sales and Marketing

During the second half of 2013, we began hiring the senior leadership of our commercial organization that is preparing our organization for the planned future launch of NUPLAZID. This commercial team is comprised of experienced professionals in marketing, reimbursement and managed markets, marketing research, commercial operations, and sales force planning and management.

We are preparing to build a specialty sales force in the U.S. of approximately 135 experienced sales professionals. If NUPLAZID is approved, this specialty sales force will focus on promoting NUPLAZID primarily to neurologists and a small group of psychiatrists and long-term care physicians who are high prescribers of antipsychotics for Parkinson's disease psychosis patients. In selected markets outside of the United States, we may choose to commercialize NUPLAZID independently or by establishing one or more strategic alliances.

Long-Lived Assets

Our long-lived assets totaled $553,000 and $579,000 as of December 31, 2014 and 2013, respectively. All of our long-lived assets are located in the United States.

Employees

At December 31, 2014, we had 97 employees. Of our total workforce, 52 are engaged in research and development activities, 31 are engaged in administrative activities such as finance, legal, and information technology, and 14 are engaged in commercial operations and marketing. 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.

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 NUPLAZID (pimavanserin) is delayed or not granted or NUPLAZID 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, import, export, 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 NUPLAZID (pimavanserin) in the United States and potentially in additional territories. The regulatory approval and successful commercialization of NUPLAZID is subject to many risks, including the risks discussed in other risk factors, and NUPLAZID 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 NUPLAZID, 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 completing the NDA and related preparations to support a review of the NDA, and plan to submit the NDA to the FDA in the first quarter of 2015. While the FDA has agreed to review an NDA for NUPLAZID on the basis of our positive pivotal -020 Study data, along with supportive efficacy and safety data from other NUPLAZID studies, the NDA will be subject to FDA review to determine whether the entire filing package is adequate to support approval of NUPLAZID for PDP. Notwithstanding the guidance that we received in April 2013, the FDA retains complete discretion in deciding whether to file an NDA for NUPLAZID and there are many components to an NDA submission beyond the efficacy and safety data reviewed by the FDA in 2013. For example, in addition to reviewing the safety and efficacy data for NUPLAZID, the FDA will review our internal systems and processes, as well as those of our vendors, related to our development of NUPLAZID, including those pertaining to our clinical trials and manufacturing processes. Even if our NDA submission for NUPLAZID is accepted for filing, the FDA retains complete discretion in deciding whether or not to approve an NDA and there is no guarantee that NUPLAZID will be approved for the treatment of PDP or any other indication. Additionally, the FDA may convene an advisory committee of independent experts, including clinicians and other scientific experts, to review, evaluate and provide recommendations as to whether the NDA for NUPLAZID should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. The FDA may choose not to approve our NDA for NUPLAZID for any of a variety of reasons, including a decision related to the safety or efficacy data for NUPLAZID or for any other issues that they may identify related to our development of NUPLAZID for the treatment of PDP.

Thus, significant uncertainty remains regarding the regulatory approval process for NUPLAZID.

Even if the FDA grants an approval for NUPLAZID for the treatment of PDP, the terms of the approval may limit its commercial potential. Additionally, even after receipt of FDA approval, NUPLAZID would be subject to substantial, ongoing regulatory requirements.

The FDA has complete discretion over the approval of NUPLAZID for the treatment of PDP. If it grants approval, the scope of the approval may limit our ability to commercialize NUPLAZID, and in turn, limit our ability to generate substantial sales revenues. For example, the FDA may not approve the labeling claims for NUPLAZID 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 manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for NUPLAZID will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with current good manufacturing practices, or cGMPs, good clinical practices, international conference on harmonization regulations and good laboratory practices, which are regulations and guidelines enforced by the FDA for all of our clinical development and for any clinical trials that we conduct post-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 NUPLAZID, 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.

Even if NUPLAZID 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 of NUPLAZID for the treatment of PDP, in addition to building a sales force, we will need to successfully coordinate the commercialization of NUPLAZID. Prior to commercialization, NUPLAZID could also be subject to review and potential scheduling by the Drug Enforcement Administration of the U.S. Department of Justice, or DEA, which could delay and 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 NUPLAZID for the treatment of PDP. If any product launch of NUPLAZID is unsuccessful or perceived as disappointing, our stock price could decline significantly and the long-term success of the product could be harmed.

We currently have no sales force and have no experience as a company in marketing or distributing pharmaceutical products. If we are unable to expand our marketing capabilities and establish our sales force or enter into agreements with third parties to distribute NUPLAZID, we may not be able to generate product revenues.

Our strategy is to build a fully-integrated biopharmaceutical company to successfully execute the commercial launch of NUPLAZID in the United States following regulatory approval. While we have established our core commercial team, we do not currently have a complete organization for the sales, marketing and distribution of NUPLAZID, and, as an organization, we do not have any experience commercializing pharmaceutical products. In order to market any products that may be approved by the FDA, including NUPLAZID, 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.

Included in our strategy in the United States is a plan to establish a specialty sales force to commercialize NUPLAZID for the treatment of PDP. The establishment and development of our own sales force to market NUPLAZID will be expensive and time consuming and could delay any product launch, and we cannot be certain that we will be able to successfully develop this capability. We will also have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain marketing and sales personnel. To the extent we rely on third parties to commercialize NUPLAZID, we may receive less revenues than if we commercialized these products ourselves. In addition, we may have little or no control over the sales efforts of any third parties involved in commercializing our products. In the event we are unable to develop our own sales force or collaborate with a third-party marketing and sales organization, we would not be able to effectively commercialize NUPLAZID which would negatively impact our ability to generate product revenues.

If we are unable to effectively train and equip our sales force, our ability to successfully commercialize NUPLAZID will be harmed.

If approved, NUPLAZID will be a newly-marketed drug and, therefore, none of the members of our sales force will have ever promoted NUPLAZID prior to its launch. As a result, we will be required to expend significant time and resources to train our sales force to be credible and persuasive in marketing NUPLAZID for the treatment of PDP to neurologists, pharmacists and long-term care facilities. In addition, we must train our sales force to ensure that a consistent and appropriate message about NUPLAZID is being delivered to our potential customers. If we are unable to effectively train our sales force and equip them with effective materials, including medical and sales literature to help them inform and educate potential customers about the benefits of NUPLAZID and its proper administration, our efforts to successfully commercialize NUPLAZID could be put in jeopardy, which would negatively impact our ability to generate product revenues.

NUPLAZID may not gain acceptance among physicians, patients, and the medical community, thereby limiting our potential to generate revenues.

Even if a product is 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 a product 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.

With respect to NUPLAZID specifically, even if approved by the FDA for the treatment of PDP, successful commercialization will depend on whether and to what extent physicians, long-term care facilities and pharmacies, over whom we have no control, determine to utilize NUPLAZID. NUPLAZID, if approved by the FDA, would be made available to treat PDP, an indication for which the FDA has not approved a pharmaceutical treatment. Because of this, it is particularly difficult to estimate NUPLAZID's market potential. Industry sources and analysts have a divergence of estimates for the near- and long-term market potential of NUPLAZID, and a variety of assumptions directly impact the estimates for NUPLAZID's market potential, including assumptions regarding the prevalence of PDP, the rate of diagnosis of PDP, the rate of physician adoption of NUPLAZID, and

patient adherence and compliance rates. Small differences in these assumptions can lead to widely divergent estimates of the market potential of NUPLAZID. For example, certain research suggests that patients with Parkinson's disease may be hesitant to report symptoms of PDP to their treating physicians for a variety of reasons, including apprehension about societal stigmas relating to mental illness. Research also suggests that physicians who typically treat patients with Parkinson's disease may not ask about or identify symptoms of PDP. For these reasons, even if PDP occurs in high rates among patients with Parkinson's disease, it may be underdiagnosed. Even if PDP is diagnosed, physicians may not prescribe treatment for it, and if they do prescribe treatment, they may prescribe other drugs to treat it, even though they are not approved for PDP, instead of NUPLAZID. In addition, even if NUPLAZID is prescribed for the treatment of PDP, issues may arise with respect to patient adherence and compliance rates. It is anticipated that the recommended dosing of NUPLAZID, if approved, will be two 17 mg tablets taken together once a day. Patients may elect, whether at the direction of their physician or otherwise, to take only one tablet a day instead of two, to take tablets at different times during the day, or to otherwise not adhere to the recommended dosing, any of which could result in far lower efficacy. If patients do not adhere to the recommended dosing of NUPLAZID, patients and physicians may believe that NUPLAZID is less effective, and as a result they may stop taking it and prescribing it. The commercial success of NUPLAZID depends on acceptance by patients and physicians, and there are a number of factors that could skew our or others' estimates about whether and to what extent NUPLAZID will be prescribed for the treatment of PDP.

Our ability to generate product revenues will be diminished if NUPLAZID does not receive coverage from payors or sells 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. Coverage and adequate 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 NUPLAZID, or other products we may market, the resulting reimbursement payment rates might not be adequate or may require co-payments that patients find unacceptably high. Patients may not use NUPLAZID if coverage is not provided or reimbursement is inadequate to cover a significant portion of the cost of those products.

In addition, the market for NUPLAZID 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, NUPLAZID or any other products we may market 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 NUPLAZID, or any other products we may market, 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, including NUPLAZID, as 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 administrative, civil and/or criminal penalties, damages, fines, individual imprisonment, 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, including NUPLAZID, 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, including NUPLAZID. 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, including NUPLAZID.

If our operations are found to be in violation of any of the laws or regulations described above, comparable laws and regulations of non-U.S. jurisdictions or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our ability to operate our business and our financial results. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

If we receive marketing approval from the FDA for NUPLAZID for the treatment of PDP, we could face liability if a regulatory authority determines that we are promoting "off-label" use.

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 made in the physician's independent medical judgment, 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 NUPLAZID, or any other 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. A significant number of pharmaceutical companies have been the target of inquiries and investigations by various U.S. federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for unapproved uses and other sales practices, including the Department of Justice and various U.S. Attorneys' Offices, the Office of Inspector General of the Department of Health and Human Services, the FDA, the Federal Trade Commission and various state Attorneys General offices. These investigations have alleged violations of various U.S. federal and state laws and regulations, including claims asserting antitrust violations, violations of the Food, Drug and Cosmetic Act, the federal False Claims Act, the Prescription Drug Marketing Act, anti-kickback laws, and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and/or Medicaid reimbursement. If the FDA or any other governmental agency initiates an enforcement action against us or if we are the subject of a *qui tam* suit and it is determined that we violated prohibitions relating to the promotion of products for unapproved uses, we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and corporate integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Any such fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects and reputation.

We expect our net losses to continue for at least the next few 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, 2014, we had an accumulated deficit of approximately $498.1 million. We expect to incur net losses over the next few 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 NUPLAZID for the treatment of PDP in the first quarter of 2015. The regulatory approval process is time consuming and uncertain and there is no guarantee that our planned NDA submission for NUPLAZID will be accepted for filing or, if accepted, approved for marketing. Even if our NDA for NUPLAZID is approved, we would still expect to incur significant expenses and net losses for at least the next few years as we begin our first ever commercialization efforts and pursue the development and commercialization of NUPLAZID and other product candidates. Substantially all of our revenues for the twelve months ended December 31, 2014 were from our agreements with various 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 significant payments from Allergan pursuant to our continuing collaborations are dependent upon the advancement of an applicable product candidate. 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.

If we fail to obtain the capital necessary to fund our operations, we will be unable to successfully develop and commercialize NUPLAZID or any of our other product candidates.

We have consumed substantial amounts of capital since our inception. Our cash, cash equivalents and investment securities totaled $322.5 million at December 31, 2014. While we believe that our existing cash resources will be sufficient to fund our cash requirements at least into the second half of 2016, we may 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 ongoing and planned development activities for pimavanserin, planned commercialization activities for NUPLAZID, and other research and development programs;
- the costs of preparing applications for regulatory approvals for NUPLAZID and other product candidates;
- the costs of establishing, or contracting for, sales and marketing capabilities for NUPLAZID or other product candidates;
- our ability to obtain regulatory approval for, and generate product sales from, NUPLAZID or other product candidates;
- the costs of acquiring additional product candidates or research and development programs;
- 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 NUPLAZID or other product candidates; and
- the costs associated with litigation.

Unless and until we can generate significant cash from our operations, 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.

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 we will need to satisfy to submit NUPLAZID 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, including that of NUPLAZID.

The pivotal Phase III study with NUPLAZID 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 NUPLAZID for the treatment of PDP. Following our April 2013 meeting with the FDA, we conducted customary supportive studies, such as drug-drug interaction studies and CMC development that 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 for FDA review of an NDA submission or of any post-approval studies that we may undertake. 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 had 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 or that future results of studies of NUPLAZID for the treatment of PDP will be consistent with those from the -020 Study.

If we do not successfully complete development of NUPLAZID, we will be unable to market and sell NUPLAZID or products derived from it, or to generate related product revenues.

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 preparations for FDA review of NUPLAZID for the treatment of PDP and clinical trials of pimavanserin for other indications, 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, and to conduct further development activities, if we do not secure a partner. Following any potential approval by the FDA, our current strategy is to commercialize NUPLAZID for PDP in the United States by establishing a specialty sales force focused primarily on neurologists and a small group of psychiatrists and long-term care physicians who are high prescribers of antipsychotics for PDP patients. In addition, if we commercialize NUPLAZID 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 NUPLAZID.

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, NUPLAZID. Following the reporting of successful results from the Phase III -020 Study with NUPLAZID in November 2012 and our meeting with the FDA in April 2013, we are completing preparations needed to support FDA review of NUPLAZID prior to our planned submission of an NDA for NUPLAZID for PDP in the first quarter of 2015. An unfavorable outcome in any of the foregoing development efforts for NUPLAZID would be a major set-back for the program and for us, generally. In particular, an unfavorable outcome in our NUPLAZID 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, 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; and
- 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;
- imposition of clinical holds by regulatory authorities or institutional review boards;
- 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.

We depend on collaborations with third parties to develop and commercialize selected product candidates other than pimavanserin, and we have limited control over how those third parties conduct development and commercialization activities for such product candidates.

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, other than pimavanserin, and we have limited control over the amount and timing of resources that our collaborators may devote to our product candidates. We may choose to rely on collaborations in the future for certain portions of our pimavanserin program or for the commercialization of NUPLAZID in certain territories outside of the United States. Our 2003 research agreement with Allergan ended in March 2013, and additional payments from our two ongoing agreements with Allergan, other than payments for a portion of patent costs for these collaborations, are dependent upon further advancement of our applicable product candidates. Unless these milestones are met, we will not receive significant 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.

In July 2014, Allergan announced that it would be reducing its worldwide headcount by approximately 13% and that it would be restructuring its operations. In November 2014, Allergan announced that it entered into

an agreement with Actavis plc under which Actavis will acquire Allergan. Allergan has also previously announced that it is seeking a partner for further development and commercialization of drug candidates in our chronic pain program. In connection with Actavis' acquisition of Allergan, or Allergan's planned restructuring, substantially less resources could be devoted to the programs covered by our collaborations with Allergan or such programs could be discontinued entirely. If Allergan is unable to successfully partner our chronic pain 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 programs to date. In addition, Allergan can terminate our existing collaborations upon prior notice to us. Allergan may be more likely to terminate, or decline to continue, some or all of our existing collaborations in connection with Actavis' acquisition of Allergan or Allergan's planned restructuring.

If Allergan elects to devote substantially less resources to the programs covered by our collaborations, absent circumstances giving rise to our right to terminate, our remedies against Allergan are limited, and we may not be able to regain rights to such programs. If Allergan elects to discontinue one or more of our programs and terminate our collaboration agreements, the discontinued programs may revert to us, in which case we would need to evaluate whether to continue advancing such programs alone or with a new collaborator. Either advancing such programs alone or seeking a new collaborator would divert our management's attention and involve expending additional resources that are currently devoted to our other programs, including our pimavanserin program.

We also face competition in our search for new collaborators, if we seek a new partner for our pimavanserin program or other programs, including any programs that may revert to us from Allergan. Given the current economic environment, it is possible that competition for new collaborators may increase. If we are unable to find new collaborations, we may not be able to continue advancing our programs alone.

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 or reduction 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 may also pursue other research programs related to pain management that are independent from our collaboration in this therapeutic area. In November 2014, Allergan announced that it entered into an agreement with Actavis under which Actavis will acquire Allergan. Actavis may have, or acquire rights to, additional programs related to chronic pain or ophthalmic diseases, including glaucoma, which could impact Allergan's strategy with respect to the development of product candidates covered by our collaborations.

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.

Of the large number of product candidates in development, only a small percentage result in the submission of an NDA to the FDA or comparable regulatory filing to regulatory authorities in other jurisdictions, and even fewer are approved for marketing. 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.

We currently depend, and will in the future continue to depend, on third parties to manufacture NUPLAZID and our other product candidates. If these manufacturers fail to provide us and our collaborators with adequate supplies of clinical trial materials and commercial product or fail to comply with the requirements of regulatory authorities, we may be unable to develop or commercialize NUPLAZID or our other product candidates.

We have no manufacturing facilities and only limited experience as an organization 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 NUPLAZID, for clinical trials. If any of our product candidates, including NUPLAZID, 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.

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 NUPLAZID, if 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. Even if we are able to enter into long-term agreements with manufacturers for commercial supply on reasonable terms, we may be unable to do so with sufficient time prior to launch of NUPLAZID, which would expose us to substantial supply risk and potentially jeopardize our launch.

The manufacturers of our product candidates are obliged to operate in accordance with FDA-mandated current good manufacturing practices, or cGMPs, and we have no control over the ability of third-party manufacturers to maintain adequate quality control, quality assurance and qualified personnel to ensure compliance with cGMPs. In addition, the facilities used by our 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. If any of our third-party manufacturers are unable to successfully manufacture material that conforms to our specifications and the FDA's strict regulatory requirements, or pass regulatory inspection, they will not be able to secure or maintain approval for the manufacturing facilities. Additionally, a failure by any of our third-party 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, including NUPLAZID, or the ultimate launch of NUPLAZID or any other products based on our product candidates. 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.

Even if we successfully enter into long-term agreements with manufacturers, the FDA may not approve the facilities of such manufacturers, the manufacturers may not perform as agreed, or the manufacturers may terminate their agreements with us. Presently, we only have one supplier for our active pharmaceutical ingredient and one supplier of tablets for our NUPLAZID (pimavanserin) program. If any of the foregoing circumstances occur, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market NUPLAZID or any of our other product candidates. While we believe that there will be alternative sources available to manufacture our product candidates, including NUPLAZID, 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.

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical

products often encounter difficulties in production, particularly in scaling up and validating initial production. These problems include difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, shortages of qualified personnel, as well as compliance with strictly-enforced federal, state and foreign regulations. We cannot assure you that any issues relating to the manufacture of any of our product candidates, including NUPLAZID, will not occur in the future. Additionally, our manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If our manufacturers were to encounter any of these difficulties, or otherwise fail to comply with their contractual obligations, our ability to commercialize NUPLAZID in the United States, or provide any product candidates to patients in clinical trials, would be jeopardized. Any delay or interruption in our ability to meet commercial demand for our products will result in the loss of potential revenues and could adversely affect our ability to gain market acceptance for these products. In addition, any delay or interruption in the supply of clinical trial supplies could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely.

Failures or difficulties faced at any level of our supply chain could materially adversely affect our business and delay or impede the development and commercialization of any of our products or product candidates and could have a material adverse effect on our business, results of operations, financial condition and prospects.

If we are unable to attract, retain, and motivate key management, research and development, and sales and marketing personnel, our drug development programs, our research and discovery efforts, and our commercialization plans may be delayed and we may be unable to successfully develop or commercialize our product candidates, including NUPLAZID.

Our success depends on our ability to attract, retain, and motivate highly qualified management, scientific, and commercial 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. Many of the other biotechnology and pharmaceutical companies with whom we compete for qualified personnel have greater financial and other resources, different risk profiles and longer histories in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high quality candidates than that which we have to offer. If we are unable to continue to attract and retain high quality personnel, the rate and success at which we can develop and commercialize products and product candidates will be limited. If we are unable to attract and retain the necessary personnel, it will significantly impede the achievement of our research and development objectives, our commercialization efforts for NUPLAZID, 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 have recently increased the size of our organization, and will need to continue to increase the size of our organization. We may encounter difficulties with managing our growth, which could adversely affect our results of operations.

As of December 31, 2014, we employed 97 full-time employees. As we advance our program towards submitting an NDA for NUPLAZID for the treatment of PDP, we already have added several capabilities. However, we will need to add qualified personnel and resources if the NDA for NUPLAZID 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 NUPLAZID. Future growth will impose significant added responsibilities on members of management, including the need to identify, recruit, maintain and integrate additional employees, and may take time away from running other aspects of our business, including development and commercialization of our product candidates.

Our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. In particular, as our commercialization plans and strategies develop, we will need to recruit and train a substantial number of sales and marketing personnel and expect to need to expand the size of our employee base for managerial, operational, financial and other resources. To that end, we must be able to:

- manage our development efforts effectively;
- integrate additional management, administrative and manufacturing personnel;
- build a marketing and sales organization; and
- maintain sufficient administrative, accounting and management information systems and controls.

We may not be able to accomplish these tasks or successfully manage our operations and, accordingly, may not achieve our research, development, and commercialization goals. Our failure to accomplish any of these goals could harm our financial results and prospects.

If we fail to develop, acquire or in-license other product candidates or products, our business and prospects would be limited. Even if we obtain rights to other product candidates or products, we will incur a variety of costs and may never realize the anticipated benefits.

A key element of our strategy is to develop, acquire or in-license businesses, technologies, product candidates or products that we believe are a strategic fit with our business. The success of this strategy depends in large part on the combination of our regulatory, development and commercial capabilities and expertise and our ability to identify, select and acquire or in-license clinically-enabled product candidates for the treatment of neurological disorders, or for therapeutic indications that complement or augment our current product candidates, or that otherwise fit into our development or strategic plans on terms that are acceptable to us. Identifying, selecting and acquiring or in-licensing promising product candidates requires substantial technical, financial and human resources expertise, and 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. Efforts to do so may not result in the actual acquisition or in-license of a particular product candidate, potentially resulting in a diversion of our management's time and the expenditure of our resources with no resulting benefit. If we are unable to identify, select and acquire or license suitable product candidates from third parties on terms acceptable to us, our business and prospects will be limited. In particular, if NUPLAZID is approved for marketing and we are unable to add additional commercial products to our portfolio, we may not be able to successfully leverage our commercial organization.

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. Moreover, any product candidate we identify, select and acquire or license may require additional, time-consuming development or regulatory efforts prior to commercial sale, including preclinical studies, if applicable, and extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to the risk of failure that is inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and/or effective for approval by regulatory authorities. In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically, successfully commercialized or

widely accepted in the marketplace or be more effective or desired than other commercially available alternatives.

In addition, if we fail to successfully commercialize and further develop NUPLAZID or our other product candidates, there is a greater likelihood that we will fail to successfully develop a pipeline of other product candidates, and our business and prospects would therefore be harmed.

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 NUPLAZID. 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, as noted above, 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 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:

- whether and when we obtain FDA approval of NUPLAZID for the treatment of PDP;
- the success of our launch and commercialization of NUPLAZID, if approved, in the United States for the treatment of PDP;
- the status of development and commercialization of pimavanserin for indications other than PDP and in jurisdictions other than the United States;
- the status of development and commercialization of our other product candidates, including compounds being developed under our collaborations;
- whether we acquire or in-license additional product candidates or products, and the status of development and commercialization of such product candidates or products;
- 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 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 Stock 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.

We will need to obtain final FDA approval of our proposed product name for pimavanserin, NUPLAZID, 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 provide final approval of the NUPLAZID product name regardless of our 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 does not approve the name NUPLAZID, 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.

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 intellectual property rights to our product candidates, including NUPLAZID, and technologies, as well as successfully defending these rights against third-party challenges. Any misappropriation of our intellectual property could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market. To protect our intellectual property, we rely on a combination of patents, trade secret protection and confidentiality agreements.

With regard to patents, although we have filed numerous patent applications worldwide with respect to pimavanserin, not all of our patent applications resulted in an issued patent, or they resulted in an issued patent that is susceptible to challenge by a third party. Our ability to obtain, maintain, and/or defend our patents covering 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 develop similar or alternative technologies or design around our patent claims to produce competitive products that fall outside of the scope of our patents;
- our disclosures in patent applications may not be sufficient to meet the statutory requirements for patentability;
- 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 are easily susceptible to challenges by third parties;
- our proprietary technologies may not be patentable;

- changes to patent laws that limit the exclusivity rights of patent holders or make it easier to render a patent invalid;
- recent decisions by the United States Supreme Court limiting patent-eligible subject matter;
- the passage of the America Invents Act (2012) introduced new procedures for challenging pending patent applications and issued patents; and
- technology that we may in-license may become important to some aspects of our business, however, we generally would not control the patent prosecution, maintenance or enforcement of any such in-licensed technology.

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 freedom to operate. Moreover, 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. For applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third-party or instituted by the United States Patent and Trademark Office, or United States PTO, to determine who was the first to invent the invention at issue. It is difficult to determine how such disputes would be resolved. Applications containing a claim not entitled to priority before March 16, 2013, are not subject to interference proceedings due the change brought by the America Invents Act (2012) to a “first to file” system. However, a derivation proceeding can be brought by a third-party alleging that the inventor derived the invention from another.

Periodic maintenance fees on any issued patent are due to be paid to the United States PTO and foreign patent agencies in several stages over the lifetime of the patent. The United States PTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

Some of our academic institutional licensors, research collaborators and scientific advisors have rights to publish data and information to which we have rights. We generally seek to prevent our collaborators from disclosing scientific discoveries until we have the opportunity to file patent applications on such discoveries, but in some cases, we are limited to relatively short periods to review a proposed publication and file a patent application. 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.

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. We also have not entered into any noncompete agreements with any of our employees. 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 future employment with any of our competitors. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results and financial condition.

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 a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including post-issuance review proceedings before the United States PTO or oppositions and other comparable proceedings in foreign jurisdictions. Post-issuance proceedings in the United States PTO, including without limitation inter partes review and post-grant review, allow third parties to challenge the validity of an issued patent in front of the United States PTO Patent Trial and Appeal Board as opposed to a federal district court. With few limitations, any third party can petition the United States PTO for inter partes review at any time for any issued patent based on prior art patents or printed publications. If it is within nine months of the issuance of the challenged patent, a third party can petition the United States PTO for post-grant review, which can be based on any invalidity grounds and is not limited to prior art patents or printed publications.

In post-issuance proceedings, United States PTO rules and regulations generally tend to favor patent challengers over patent owners. For example, unlike in district court litigation, claims challenged in post-issuance proceedings are given their broadest reasonable meaning, which increases the chance a claim might be invalidated by prior art or lack support in the patent specification. And, unlike in district court litigation, there is no presumption of validity for an issued patent. As a result of these rules and others, statistics released by the United States PTO show a high percentage of claims being invalidated in post-issuance proceedings. Moreover, with few exceptions, there is no standing requirement to petition the United States PTO for inter partes review or post-grant review. In other words, companies that have not been charged with infringement or that lack commercial interest in the patented subject matter can still petition the United States PTO for review of an issued patent. Thus, even where we have issued patents, our rights under those patents may be challenged and ultimately not provide us with sufficient protection against competitive products or processes.

While we are not currently subject to any pending intellectual property litigation or patent challenges, and are not aware of any such threatened litigation or patent challenges, 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, and such patents are held to be valid and enforceable, 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, and such patents are held to be valid and enforceable, 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, which could potentially be trebled 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.

Furthermore, because of the substantial amount of pre-trial document and witness discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, during the course of this kind of litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the trading price of our common stock.

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 strength of patents in the pharmaceutical and biotechnology field can be highly uncertain and involve complex legal and factual questions. For example, some of our patent applications may cover the uses of gene sequences. The patentability of gene sequences and the use of gene sequences has been seriously undermined by recent decisions of the United States Supreme Court. The United States PTO's interpretation of the Supreme Court's decisions and the standards for patentability it sets forth 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 as mentioned above, and U.S. patents may be subject to reexamination and post-issuance proceedings in the United States PTO (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, post-issuance 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 America Invents Act (2012) included a number of significant changes to U.S. patent law. These included 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. It is still not clear what, if any, impact the America Invents 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, including NUPLAZID, 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, including NUPLAZID, 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 and, similarly, 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, including NUPLAZID, 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 NUPLAZID for the treatment of PDP would compete with off-label use of antipsychotic drugs, including Seroquel, marketed by Astra-Zeneca PLC, and with the generic drug clozapine. Our potential products for the treatment of schizophrenia would compete with Latuda, marketed by Sunovion Pharmaceuticals Inc., Zyprexa, marketed by Eli Lilly and Company, Risperdal, marketed by Johnson & Johnson, Abilify, marketed jointly by Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co., Ltd., Seroquel, and clozapine. Our potential product for the treatment of ADP would compete with Risperdal and with off-label use of antipsychotic drugs and drugs indicated for the treatment of Alzheimer's disease and dementia in patients with Alzheimer's disease, including Aricept, marketed by Eisai Inc. and Pfizer Inc., and Namenda, marketed by Forest Laboratories, LLC, a wholly-owned subsidiary of Actavis. 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 historically has been, and is likely to remain, highly volatile.

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, including NUPLAZID, 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 NUPLAZID;
- 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 products, or other material events by our competitors or us, including any new products that we may acquire or in-license;
- 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 Stock 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 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. In addition, in connection with our March 2014 public offering of common stock, we agreed to provide resale registration rights for the shares of our common stock held by entities affiliated with one of our principal stockholders and one of our directors, Dr. Stephen R. Biggar. 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 statement, or an indeterminate number of shares 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 66⅔ 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.***

As of December 31, 2014, 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.

Effective November 13, 2014, we entered into a sublease agreement for approximately 51,000 square feet of office space located in San Diego, California. The term of the lease is expected to run from January 2015 through February 2019. Including this new lease, 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 Select 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 Select Market for the periods indicated.

2014	**High**	**Low**
First Quarter	$32.00	$21.20
Second Quarter	$25.50	$15.64
Third Quarter	$29.31	$19.21
Fourth Quarter	$33.49	$22.04
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

As of February 9, 2015, there were approximately 40 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, 2014 and 2013 and the related consolidated statements of operations for each of the three years ended December 31, 2014 and related notes appearing elsewhere in this report. The statement of operations data for the years ended December 31, 2011 and 2010 and the balance sheet data as of December 31, 2012, 2011 and 2010 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,				
	2014	2013	2012	2011	2010 (1)
	(in thousands, except per share data)				
Consolidated Statement of Operations Data:					
Revenues:					
Collaborative revenues	$ 120	$ 1,145	$ 4,907	$ 2,067	$42,135
Operating expenses:					
Research and development	60,602	26,722	18,794	17,309	20,579
General and administrative	32,748	12,720	6,999	7,610	6,462
Total operating expenses	93,350	39,442	25,793	24,919	27,041
Income (loss) from operations	(93,230)	(38,297)	(20,886)	(22,852)	15,094
Interest income, net	755	349	37	87	45
Net income (loss)	$(92,475)	$(37,948)	$(20,849)	$(22,765)	$15,139
Net income (loss) per common share, basic	$ (0.95)	$ (0.44)	$ (0.38)	$ (0.44)	$ 0.39
Net income (loss) per common share, diluted	$ (0.95)	$ (0.44)	$ (0.38)	$ (0.44)	$ 0.39
Weighted average shares used in computing net income (loss) per common share, basic	97,248	85,715	55,116	52,183	38,593
Weighted average shares used in computing net income (loss) per common share, diluted	97,248	85,715	55,116	52,183	38,720

(1) 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,				
	2014	2013	2012	2011	2010
	(in thousands)				
Consolidated Balance Sheet Data:					
Cash, cash equivalents and investment securities	$322,486	$185,790	$107,967	$31,048	$37,087
Working capital	308,784	181,381	102,600	25,784	31,890
Total assets	325,458	189,118	108,590	32,114	38,394
Long-term debt, less current portion	—	—	—	—	32
Total stockholders' equity	309,489	182,131	84,984	23,362	29,688

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," "predicts," "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 medicines that address unmet medical needs in neurological and related central nervous system disorders. We have a portfolio of product opportunities led by our novel drug candidate, NUPLAZID (pimavanserin), for which we have reported positive Phase III pivotal trial results in Parkinson's disease psychosis, or PDP, and which has the potential to be the first drug approved in the United States for this disorder. We are currently completing a New Drug Application, or NDA, and related preparations to support a review of the NDA by the U.S. Food and Drug Administration, or FDA. We plan to submit the NDA to the FDA in the first quarter of 2015. 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.

We are pursuing Parkinson's disease psychosis as our lead indication for NUPLAZID. We have completed a successful pivotal Phase III trial with NUPLAZID 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 NUPLAZID, are sufficient to support the filing of an NDA for the treatment of PDP. In September 2014, we announced that the FDA has granted Breakthrough Therapy designation for NUPLAZID for the treatment of Parkinson's disease psychosis. The Breakthrough Therapy designation was created by the FDA to expedite the development and review of drugs that are intended to treat serious or life-threatening conditions. If approved, we intend to commercialize NUPLAZID for Parkinson's disease psychosis in the United States by establishing a specialty sales force focused primarily on neurologists and a small group of psychiatrists and long-term care physicians who are high prescribers of antipsychotics for PDP patients. Starting in the second half of 2013, we began to hire the senior leadership of our commercial organization. We are currently preparing for the planned future launch of NUPLAZID and plan to hire a commercial sales force to coincide approximately with a NUPLAZID approval, if any. In addition to building our commercial capabilities, we are expanding our existing infrastructure to support the planned launch and commercialization of NUPLAZID, including adding to our commercial level manufacturing, medical affairs, quality control, and compliance capabilities.

We believe that pimavanserin also has the potential to address 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 next plan to evaluate the use of pimavanserin as a stand-alone maintenance therapy between acute psychotic episodes in a Phase II schizophrenia study.

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, 2014, we had an accumulated deficit of $498.1 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 opportunities.

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, 2014, we had received an aggregate of $115.8 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 net 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.

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 pimavanserin. Historically, 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 by project for the years ended December 31, 2014, 2013, and 2012 (in thousands):

	Years Ended December 31,		
	2014	2013	2012
Costs of external service providers:			
NUPLAZID (pimavanserin)	$43,161	$16,625	$12,401
Other programs	723	709	932
Subtotal	43,884	17,334	13,333
Internal costs	11,527	7,180	4,781
Stock-based compensation	5,191	2,208	680
Total research and development	$60,602	$26,722	$18,794

While we intend to submit an NDA to the FDA for NUPLAZID in the first quarter of 2015, at this time, due to the risks inherent in the regulatory and approval processes, we are unable to estimate with any certainty the costs we will incur for the continued development of NUPLAZID 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, including Alzheimer's disease psychosis and schizophrenia. 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 preparing to support a review of the NDA by the FDA, and advancing the development of pimavanserin for other indications, 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 opportunities 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 remaining preparations that are needed to support the FDA review of NUPLAZID for Parkinson's disease psychosis for which we plan to submit an NDA in the first quarter of 2015, our ongoing open-label safety extension study, our ongoing Phase II trial for Alzheimer's disease psychosis, and potential studies in other indications, including schizophrenia. The lengthy process of completing clinical trials and supporting development activities and seeking regulatory approval for our product opportunities 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, starting in the second half of 2013, we began to hire the senior leadership of our commercial organization that is helping us prepare for the planned future launch of NUPLAZID and we are currently preparing to build a specialty sales force in the U.S. that will focus on promoting NUPLAZID, if approved by the FDA. We expect our general and administrative expenses to increase in future periods to support activities associated with our preparation for, and planned launch of, NUPLAZID and our further development of pimavanserin in indications other than Parkinson's disease psychosis.

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 valuation 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, 2014 and 2013

Revenues

Revenues decreased to $120,000 in 2014 from $1.1 million in 2013. This decrease was partially due to the conclusion of our 2003 research collaboration with Allergan in March 2013. Revenues from our collaborations with Allergan decreased to $40,000 in 2014 from $571,000 in 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. Additionally, revenues from our agreements with other parties, including our research grants, decreased to $80,000 in 2014 compared to $574,000 in 2013 due to decreased activities under research grants.

Research and Development Expenses

Research and development expenses increased to $60.6 million in 2014, including $5.2 million in stock-based compensation, from $26.7 million in 2013, including $2.2 million in stock-based compensation. This increase was primarily due to an increase of $26.6 million in external service costs as well as an increase in costs associated with our expanded research and development organization, including $4.2 million in increased personnel costs, and $3.0 million in increased stock-based compensation. External service costs totaled $43.9 million, or 72 percent of our research and development expenses, in 2014, compared to $17.3 million, or 65 percent of our research and development expenses, in 2013. The increase in external service costs was largely attributable to increased third-party costs related to our development of, and planned NDA submission for, NUPLAZID. We expect our research and development expenses to increase in future periods as we continue to pursue the development of pimavanserin, including remaining preparations that are needed to support the FDA review of our planned NDA for NUPLAZID, our ongoing open-label safety extension study, our ongoing 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 $32.7 million in 2014, including $10.8 million in stock-based compensation, from $12.7 million in 2013, including $3.5 million in stock-based compensation. The increase in general and administrative expenses was primarily due to an increase in costs associated with additional administrative and commercial personnel, including $7.3 million in increased stock-based compensation, and $4.7 million in increased personnel expenses, as well as an increase of $6.7 million in external service costs. The increase in external service costs was largely attributable to increased consulting and professional fees 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 NUPLAZID.

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.

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.

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, 2014, we had received $755.3 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, $115.8 million in payments from collaboration agreements, $23.3 million in interest income, and $22.4 million in debt financing.

At December 31, 2014, we had $322.5 million in cash, cash equivalents, and investment securities compared to $185.8 million at December 31, 2013. We anticipate that the level of cash used in our operations will increase in future periods in order to fund our planned NDA-enabling work and commercial activities for NUPLAZID and our ongoing and planned development activities for pimavanserin for other indications. We expect that our cash, cash equivalents, and investment securities will be sufficient to fund our planned operations at least into the second half of 2016.

We may 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 ongoing and planned development activities for pimavanserin, planned commercialization activities for NUPLAZID, and other research and development programs;
- the costs of preparing applications for regulatory approvals for NUPLAZID and other product opportunities;
- our ability to obtain regulatory approval for, and generate product sales from NUPLAZID or other products;
- the costs of establishing, or contracting for, sales and marketing capabilities for NUPLAZID or other product opportunities;
- 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 NUPLAZID or other product opportunities.

Unless and until we can generate significant cash from our operations, we expect to satisfy our future cash needs through our existing cash resources, public or private sales of our equity securities, debt financings, grant funding, strategic collaborations, or by otherwise 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 NUPLAZID (pimavanserin) program could have a material adverse effect on our ability to raise additional capital.

If we need but 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

disruptions in the credit markets that have occurred in the past. However, if there are future disruptions in the credit markets, there can be no assurance that our investment portfolio will not be adversely affected.

Net cash used in operating activities increased to $66.4 million in 2014 compared to $31.8 million in 2013 and $21.6 million in 2012. The increase in net cash used in operating activities in 2014 relative to 2013 was primarily due to the increase in our net loss, offset by an increase of $10.3 million in non-cash stock-based compensation expense, together with changes in our operating assets and liabilities, including accounts payable and accrued expenses. Accounts payable and accrued expenses increased by $8.9 million in 2014 compared to an increase of $1.4 million during 2013. The increase in accounts payable and accrued expenses was primarily due to an increase in external service costs associated with our expanded research and development activities.

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 from 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.

Net cash used in investing activities totaled $87.3 million in 2014 compared to $126.1 million in 2013 and $25.5 million in 2012. Net cash used in investing activities has fluctuated significantly from period to period primarily due to the timing of purchases and maturities of investment securities. The decrease in net cash used in investing activities in 2014 relative to 2013 was primarily due to increased maturities of investment securities relative to purchases 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.

Net cash provided by financing activities increased to $203.9 million in 2014 compared to $111.7 million in 2013 and $98.2 million in 2012. The increase in net cash provided by financing activities in 2014 relative to 2013 was primarily attributable to $196.8 million in net proceeds received from our public offering of common stock in March 2014. The increase in net cash provided by financing activities in 2013 relative to 2012 was primarily due 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.

Contractual Obligations

The following table summarizes our contractual obligations at December 31, 2014 (in thousands):

	Total	Less than 1 Year	1-3 Years	4-5 Years	After 5 Years
Operating leases	$7,361	$2,119	$4,982	$260	$—

We have also entered into agreements with contract research organizations and other external service providers for services, primarily in connection with the development and planned commercialization of our product candidates. We were contractually obligated for up to approximately $16.3 million of future services under these agreements as of December 31, 2014. The nature of the work being conducted under our agreements with external service providers 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 NUPLAZID (pimavanserin). If certain conditions are met, we would be required to make future payments, including milestones, sublicensing fees, and royalties. The potential future milestone payments include $2.5 million payable upon the successful filing of the first regulatory application with the FDA and $8.0 million payable upon obtaining the first regulatory approval from the FDA. Royalty payments of up to two percent would be payable on future net product sales, if any. Because these milestone payments would only be payable upon the achievement of the 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 this agreement. Similarly, royalty payments would be contingent upon any net product sales. 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, 2014, 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, 2014, 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, 2014.

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, 2014, 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 (COSO) in Internal Control-Integrated Framework (2013). In adopting the 2013 Framework, management assessed the applicability of the principles within each component of internal control and determined whether or not they have been adequately addressed within the current system of internal control and adequately documented. 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, 2014, 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, 2014 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in its report, which appears under Item 15 in this 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 changes 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 2015 Annual Meeting of Stockholders to be filed with the SEC by April 30, 2015 (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 *http://www.acadia-pharm.com* 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:

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.

ACADIA PHARMACEUTICALS INC.

/s/ ULI HACKSELL

Uli Hacksell, Ph.D.
Chief Executive Officer

Date: February 26, 2015

KNOW ALL PERSONS BY THESE PRESENTS, that each individual whose signature appears below constitutes and appoints Uli Hacksell and Stephen R. Davis, and each of them, his true and lawful attorneys-in-fact 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 **Uli Hacksell**	Chief Executive Officer and Director (Principal Executive Officer)	February 26, 2015
/s/ STEPHEN R. DAVIS **Stephen R. Davis**	Executive Vice President, Chief Financial Officer and Chief Business Officer (Principal Financial Officer and Principal Accounting Officer)	February 26, 2015
/s/ LESLIE IVERSEN **Leslie Iversen**	Chairman of the Board	February 26, 2015
/s/ STEPHEN BIGGAR **Stephen Biggar**	Director	February 26, 2015
/s/ MICHAEL BORER **Michael Borer**	Director	February 26, 2015
/s/ LAURA BREGE **Laura Brege**	Director	February 26, 2015
/s/ MARY ANN GRAY **Mary Ann Gray**	Director	February 26, 2015
/s/ LESTER KAPLAN **Lester Kaplan**	Director	February 26, 2015
/s/ TORSTEN RASMUSSEN **Torsten Rasmussen**	Director	February 26, 2015
/s/ WILLIAM M. WELLS **William M. Wells**	Director	February 26, 2015

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, 2014 and 2013, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2014 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, 2014, based on criteria established in Internal Control—Integrated Framework (2013) 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. Our responsibility is to express opinions on these financial statements and on the Company's internal control over financial reporting based on our integrated audits. We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the 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 26, 2015

ACADIA PHARMACEUTICALS INC.

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

	December 31,	
	2014	2013
Assets		
Cash and cash equivalents	$ 61,854	$ 11,707
Investment securities, available-for-sale	260,632	174,083
Interest and other receivables	964	750
Prepaid expenses and other current assets	1,168	1,820
Total current assets	324,618	188,360
Property and equipment, net	553	579
Other assets	287	179
Total assets	$ 325,458	$ 189,118
Liabilities and stockholders' equity		
Accounts payable	$ 2,016	$ 372
Accrued expenses	13,818	6,552
Deferred revenue	—	55
Total current liabilities	15,834	6,979
Long-term liabilities	135	8
Total liabilities	15,969	6,987
Commitments and contingencies (Note 10)		
Stockholders' equity		
Preferred stock, $0.0001 par value; 5,000,000 shares authorized at December 31, 2014 and 2013; no shares issued and outstanding at December 31, 2014 and 2013	—	—
Common stock, $0.0001 par value; 150,000,000 shares authorized at December 31, 2014 and 2013; 100,047,331 shares and 91,102,618 shares issued and outstanding at December 31, 2014 and 2013, respectively	10	9
Additional paid-in capital	807,631	587,742
Accumulated deficit	(498,143)	(405,668)
Accumulated other comprehensive (loss) income	(9)	48
Total stockholders' equity	309,489	182,131
Total liabilities and stockholders' equity	$ 325,458	$ 189,118

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,		
	2014	2013	2012
Revenues			
Collaborative revenues	$ 120	$ 1,145	$ 4,907
Operating expenses			
Research and development (includes stock-based compensation expense of $5,191, $2,208, and $680, respectively)	60,602	26,722	18,794
General and administrative (includes stock-based compensation expense of $10,848, $3,503, and $1,250, respectively)	32,748	12,720	6,999
Total operating expenses	93,350	39,442	25,793
Loss from operations	(93,230)	(38,297)	(20,886)
Interest income, net	755	349	37
Net loss	$(92,475)	$(37,948)	$(20,849)
Net loss per common share, basic and diluted	$ (0.95)	$ (0.44)	$ (0.38)
Weighted average common shares outstanding, basic and diluted	97,248	85,715	55,116

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,		
	2014	2013	2012
Net loss	$(92,475)	$(37,948)	$(20,849)
Other comprehensive loss:			
Unrealized gain (loss) on investment securities	(60)	45	(4)
Foreign currency translation adjustments	3	(1)	(1)
Comprehensive loss	$(92,532)	$(37,904)	$(20,854)

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

ACADIA PHARMACEUTICALS INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Years Ended December 31,		
	2014	2013	2012
Cash flows from operating activities			
Net loss	$ (92,475)	$ (37,948)	$(20,849)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation	16,039	5,711	1,930
Amortization of premiums and accretion of discounts on investment securities, available for sale	484	1,528	(133)
Depreciation and amortization	206	79	109
Gain on disposal of assets	—	(10)	(252)
Changes in operating assets and liabilities:			
Interest and other receivables	(214)	(505)	279
Prepaid expenses and other current assets	652	(1,484)	41
Other assets	(108)	(179)	14
Accounts payable	1,644	(1,003)	(585)
Accrued expenses	7,266	2,413	635
Deferred revenue	(55)	(379)	(2,822)
Long-term liabilities	127	8	—
Net cash used in operating activities	(66,434)	(31,769)	(21,633)
Cash flows from investing activities			
Purchases of investment securities	(335,361)	(211,585)	(56,728)
Maturities of investment securities	248,268	86,087	30,948
Purchases of property and equipment	(180)	(618)	—
Proceeds from sales of property and equipment	—	12	252
Net cash used in investing activities	(87,273)	(126,104)	(25,528)
Cash flows from financing activities			
Proceeds from issuances of equity securities, net of issuance costs	203,851	111,682	98,204
Repayments of long-term debt	—	—	(32)
Net cash provided by financing activities	203,851	111,682	98,172
Effect of exchange rate changes on cash	3	(1)	(1)
Net increase (decrease) in cash and cash equivalents	50,147	(46,192)	51,010
Cash and cash equivalents			
Beginning of year	11,707	57,899	6,889
End of year	$ 61,854	$ 11,707	$ 57,899

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

ACADIA PHARMACEUTICALS INC.

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

	Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Stockholders' Equity
	Shares	Amount				
Balances at December 31, 2011	52,898,659	$ 5	$370,219	$(346,871)	$ 9	$ 23,362
Issuance of common stock and warrants, net of issuance costs	19,000,000	2	80,536	—	—	80,538
Issuance of common stock from exercise of stock options	293,595	—	453	—	—	453
Issuance of common stock pursuant to employee stock purchase plan	205,862	—	123	—	—	123
Issuance of common stock from exercise of warrants on a net issuance basis	936,100	—	—	—	—	—
Issuance of common stock under ATM Agreement, net of issuance costs	5,347,137	1	17,089	—	—	17,090
Reclassification to redeemable common stock	(5,347,137)	(1)	(17,657)	—	—	(17,658)
Net loss	—	—	—	(20,849)	—	(20,849)
Stock-based compensation	—	—	1,930	—	—	1,930
Other comprehensive loss	—	—	—	—	(5)	(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
Issuance of common stock from exercise of stock options	1,455,406	—	3,441	—	—	3,441
Issuance of common stock pursuant to employee stock purchase plan	122,853	—	358	—	—	358
Issuance of common stock from exercise of warrants on a net issuance basis	1,643,006	—	—	—	—	—
Reclassification from redeemable common stock	5,347,137	1	17,657	—	—	17,658
Net loss	—	—	—	(37,948)	—	(37,948)
Stock-based compensation	—	—	5,711	—	—	5,711
Other comprehensive income	—	—	—	—	44	44
Balances at December 31, 2013	91,102,618	$ 9	$587,742	$(405,668)	$ 48	$182,131
Issuance of common stock in public offering, net of issuance costs	7,360,000	1	196,778	—	—	196,779
Issuance of common stock from exercise of stock options	1,486,802	—	6,408	—	—	6,408
Issuance of common stock pursuant to employee stock purchase plan	97,911	—	664	—	—	664
Net loss	—	—	—	(92,475)	—	(92,475)
Stock-based compensation	—	—	16,039	—	—	16,039
Other comprehensive income	—	—	—	—	(57)	(57)
Balances at December 31, 2014	100,047,331	$ 10	$807,631	$(498,143)	$ (9)	$309,489

The accompanying notes are an integral part of these 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, 2014, the Company had an accumulated deficit of $498.1 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 may 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, including the ability of the Company to obtain regulatory approval for its products, costs associated with establishing necessary sales and marketing capabilities, the amount of product sales, if any, 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. Unless and until the Company can generate significant cash from operations, 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 needs but cannot raise adequate additional capital, it will be required to delay, 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 commercialization 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 subsidiaries located in Europe. All intercompany accounts and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of financial statements in conformity with U.S. generally accepted accounting principles ("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.

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

The Company has classified all of its investment securities as available-for-sale and, accordingly, carries these investments 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.

Fair Value of Financial Instruments

The carrying values of the Company's financial instruments, consisting of cash and cash equivalents, interest and other receivables, and accounts payable and accrued expenses, approximate fair value due to the relative short-term nature of these instruments.

As disclosed in Note 4, the Company classifies its cash equivalents and available-for-sale investment securities within the fair value hierarchy as defined by authoritative guidance:

Level 1 Inputs — Quoted prices for identical instruments in active markets.

Level 2 Inputs — Quoted prices for similar instruments in active markets; quoted prices for identical or similar instruments in markets that are not active; and model-derived valuations in which all significant inputs and significant value drivers are observable.

Level 3 Inputs — Valuation derived from valuation techniques in which one or more significant inputs or significant value drivers are unobservable.

Property and Equipment

Property and equipment are recorded at cost and depreciated over their estimated useful lives 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. Construction-in-process reflects amounts incurred for property, equipment or improvements that have not been placed in service. 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.

Estimated useful lives by major asset category are as follows:

	Useful Lives
Machinery and equipment	5 to 7 years
Computers and software	3 years
Furniture and fixtures	10 years

Impairment of Long-Lived Assets

The Company reviews its long lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by a comparison of the carrying amount of an asset to estimated undiscounted future cash flows expected to be generated by the asset. If the carrying amount of an asset exceeds its estimated future cash flows, an impairment charge is recognized by the amount by which the carrying amount of the asset exceeds the fair value of the asset. No such impairment losses have been recorded by the Company.

Revenues

The Company recognizes revenues in accordance with authoritative guidance established by 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.

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 in accordance with the Company's investment policy. The Company's investment policy defines allowable investments and establishes 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.

During the years ended December 31, 2014, 2013 and 2012, revenues from the Company's agreements with certain collaborative partners exceeded 10 percent of its total revenues. During the year ended December 31, 2014, revenues from Fast Forward, LLC and Allergan, Inc. comprised 59 percent and 33 percent of total revenues, respectively. During the year ended December 31, 2013, revenues from Allergan, 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. comprised 23 percent and 66 percent of total revenues, respectively.

The Company does not currently have any of its own manufacturing facilities, and therefore relies on third-party manufacturers to produce its product candidates for clinical trials. Although there are potential sources of supply other than the Company's existing suppliers, any new supplier would be required to qualify under applicable regulatory requirements.

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 valuation model. The estimated fair value of each stock option and purchase right, including the effect of estimated forfeitures, is then expensed over the requisite service period, which is generally the vesting period. The following assumptions were used during these periods:

	Years Ended December 31,		
	2014	2013	2012
Stock Options:			
Expected volatility	93%	94%	98-99%
Risk-free interest rate	1-2%	1-2%	1%
Expected dividend yield	0%	0%	0%
Expected life of options in years	5.7	6.0	5.8-6.0

	Years Ended December 31,		
	2014	2013	2012
Employee Stock Purchase Plan:			
Expected volatility	44-95%	69-118%	69-137%
Risk-free interest rate	0.1-0.5%	0.1-0.3%	0.1-0.3%
Expected dividend yield	0%	0%	0%
Expected life of options in years	0.5-2.0	0.5-2.0	0.5-2.0

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

Risk-Free Interest Rate. The Company determines its risk-free interest rate assumption based on the U.S. Treasury yield for obligations with contractual terms similar to the expected term of the stock option or purchase right being valued.

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.

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.

Net Loss Per Share

Net loss per share is presented as basic and diluted net loss per share. Basic net loss per share is calculated by dividing the net loss by the weighted average number of common shares outstanding for the period, without consideration for common stock equivalents. Diluted net loss per share is computed by dividing the net loss by the weighted average number of common shares and common stock equivalents outstanding for the period determined using the treasury stock method. For purposes of this calculation, stock options and warrants are considered to be common stock equivalents but are not included in the calculations of diluted net loss per share for the periods presented as their effect would be antidilutive.

Shares used in calculating basic and diluted net loss per common share exclude the following potential common shares as their effect is antidilutive (in thousands):

	Years Ended December 31,		
	2014	2013	2012
Antidilutive options to purchase common stock	7,773	7,245	6,868
Antidilutive warrants to purchase common stock	1,966	3,116	4,388
	9,739	10,361	11,256

Segment Reporting

Management has determined that the Company operates in one business segment. All revenues for the years ended December 31, 2014, 2013 and 2012 were generated in the United States.

Recently Issued Accounting Standards

In May 2014, the Financial Accounting Standards Board issued authoritative accounting guidance related to revenue from contracts with customers. This guidance is a comprehensive new revenue recognition model that requires a company to recognize revenue to depict the transfer of goods or services to a customer at an amount that reflects the consideration it expects to receive in exchange for those goods or services. This guidance is effective for annual reporting periods beginning after December 15, 2016 and early adoption is not permitted. The Company will adopt this guidance on January 1, 2017. Companies may use either a full retrospective or a modified retrospective approach to adopt this guidance. The Company is evaluating which transition approach to use and its impact, if any, on its consolidated financial statements.

In August 2014, the FASB issued authoritative accounting guidance related to an entity's ability to continue as a going concern. This guidance will explicitly require management to assess an entity's ability to continue as a going concern, and to provide related footnote disclosures in certain circumstances. The new standard is effective for annual reporting periods ending after December 15, 2016 and early adoption is permitted. The Company intends to adopt this guidance at the beginning of its first quarter of fiscal year 2016 and does not expect it to have a material impact on its consolidated financial statements and related disclosures.

3. Investment Securities

Investment securities, all classified as available-for-sale, consisted of the following (in thousands):

	December 31, 2014			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Estimated Fair Value
U.S. Treasury notes	$ 2,748	$ 2	$—	$ 2,750
Government sponsored enterprise securities	97,237	8	(10)	97,235
Corporate debt securities	137,682	3	(37)	137,648
Commercial paper	22,980	19	—	22,999
	$260,647	$32	$ (47)	$260,632

	December 31, 2013			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Estimated Fair Value
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

The Company has classified all of its available-for-sale investment securities, including those with maturities beyond one year, as current assets on its 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, 2014, all of the Company's available-for-sale investment securities had contractual maturity dates less than one year. As of December 31, 2013, the Company held $33.5 million of available-for-sale investment securities with contractual maturity dates more than one year and less than two years.

At each reporting date, the Company performs an evaluation of impairment to determine if the unrealized losses are other-than-temporary. Factors considered in determining whether a loss is other-than-temporary include the length of time and extent to which fair value has been less than the cost basis, the financial condition of the issuer, and the Company's intent and ability to hold the investment until recovery of its amortized cost basis. The Company intends, and has the ability, to hold its investments in unrealized loss positions until their amortized cost basis has been recovered. Based on its evaluation, the Company determined that its unrealized losses were not other-than-temporary at December 31, 2014 and 2013.

4. Fair Value Measurements

As of December 31, 2014, the Company held $322.1 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 in accordance with the Company's investment policy. The Company's investment policy defines allowable investments and establishes 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 obtains the fair value of its Level 2 financial instruments from third party pricing services. The pricing services utilize industry standard valuation models whereby all significant observable inputs, including benchmark yields, reported trades, broker/dealer quotes, issuer spreads, bids, offers, or other market-related data, are observable. The Company validates the prices provided by the third-party pricing services by reviewing their pricing methods and matrices, and obtaining market values from other pricing sources. After completing the validation procedures, the Company did not adjust or override any fair value measurements provided by these pricing services as of December 31, 2014 and 2013, respectively.

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.

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

	December 31, 2014	Fair Value Measurements at Reporting Date Using		
		Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents:				
Money market fund	$ 48,423	$48,423	$ —	$—
Government sponsored enterprise securities	13,000	—	13,000	—
U.S. Treasury notes	2,750	2,750	—	—
Government sponsored enterprise securities	97,235	—	97,235	—
Corporate debt securities	137,648	—	137,648	—
Commercial paper	22,999	—	22,999	—
	$322,055	$51,173	$270,882	$—

	December 31, 2013	Fair Value Measurements at Reporting Date Using		
		Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents:				
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	$14,495	$171,336	$—

5. Balance Sheet Components

Property and equipment, net, consisted of the following (in thousands):

	December 31,	
	2014	2013
Machinery and equipment	$ 896	$ 875
Computers and software	862	863
Leasehold improvements	627	570
Furniture and fixtures	244	245
Construction-in-Process	64	—
	2,693	2,553
Accumulated depreciation and amortization	(2,140)	(1,974)
	$ 553	$ 579

Depreciation and amortization of property and equipment was $206,000, $79,000, and $109,000 for the years ended December 31, 2014, 2013, and 2012, respectively. During 2014 and 2013, the Company retired $40,000 and $2.8 million, respectively, 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.

Accrued expenses consisted of the following (in thousands):

	December 31,	
	2014	2013
Accrued research and development services	$ 7,814	$4,207
Accrued compensation and benefits	4,167	1,865
Accrued consulting and professional fees	1,497	308
Other	340	172
	$13,818	$6,552

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, 2014, and is eligible to receive up to an aggregate of $15.0 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, 2014, and is eligible to receive up to an aggregate of $10.0 million in additional payments upon the achievement of development and regulatory milestones. The Company also is eligible to receive royalties on future net 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 $40,000, $571,000, and $1.1 million during each of the years ended December 31, 2014, 2013, and 2012.

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 $3.0 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 during the year ended December 31, 2012.

7. Stockholders' Equity

Public Offerings

In March 2014, the Company raised net proceeds of $196.8 million from the sale of 7,360,000 shares of its common stock in a public offering, including 960,000 shares sold pursuant to the exercise in full of the underwriters' over-allotment option.

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, 2014, 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, resulting in net proceeds of $17.1 million after issuance costs.

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, 2014, there were 12,561,435 shares of common stock authorized for issuance, of which 4,630,905 shares were 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, 2014 are presented below:

	Number of Shares	Weighted-Average Exercise Prices	Weighted Average Remaining Contractual Term
Outstanding at December 31, 2013	7,338,138	$ 6.81	
Granted	2,519,500	$25.32	
Exercised	(1,486,802)	$ 4.31	
Canceled/forfeited	(440,306)	$16.11	
Outstanding at December 31, 2014	7,930,530	$12.65	7.26
Vested and expected to vest at December 31, 2014	7,577,438	$12.19	7.17
Exercisable at December 31, 2014	4,246,262	$ 5.51	5.78

The aggregate intrinsic value of options outstanding and exercisable as of December 31, 2014, 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 $31.75. The aggregate intrinsic value of options outstanding and exercisable as of December 31, 2014, was $111.4 million. The aggregate intrinsic value of options exercised during the years ended December 31, 2014, 2013, and 2012 was approximately $30.6 million, $20.7 million, and $650,000, respectively, determined as of the date of exercise. The Company received $6.4 million in cash from options exercised during the year ended December 31, 2014.

The weighted average fair value of options granted during the years ended December 31, 2014, 2013, and 2012 was approximately $18.90, $12.66, and $1.51, respectively. As of December 31, 2014, total unrecognized compensation cost related to stock options and purchase rights was approximately $45.7 million, and the weighted average period over which this cost is expected to be recognized is 2.9 years.

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 the years ended December 31, 2014 and 2012.

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 included an "evergreen" provision providing that a limited number of additional 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 ended with the meeting in 2014. Through December 31, 2014, a total of 1,525,000 shares of common stock had been reserved for issuance under the Purchase Plan. At December 31, 2014, 385,489 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, 2014, 2013, and 2012, a total of 97,911, 122,853, and 205,862 shares of common stock were issued under the Purchase Plan at average prices of $6.78, $2.92, and $0.60, respectively. The weighted average fair value of purchase rights granted during the years ended December 31, 2014, 2013, and 2012 was $11.09, $10.96, and $2.43, respectively. During the years ended December 31, 2014, 2013, and 2012, the Company recorded cash received from the exercise of purchase rights of $664,000, $358,000, and $123,000, respectively.

Common Stock Reserved for Future Issuance

At December 31, 2014, a total of 7,930,530 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 $489,000, $240,000, and $180,000 for the years ended December 31, 2014, 2013, and 2012, respectively.

9. Income Taxes

At December 31, 2014, the Company had both federal and state net operating loss ("NOL") carryforwards of approximately $462.8 million and $431.7 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 previously 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 reduced its deferred tax assets related to the federal 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 were 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. The Company completed a study through December 31, 2014 during the current year and concluded no additional ownership changes occurred. 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 $17.9 million will expire in 2018 and 2015, respectively, unless utilized. The remaining federal and state NOL carryforwards will begin to expire in 2019 and 2016, respectively. At December 31, 2014, the Company had $9.7 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, 2014, the Company had $6.1 million of state R&D credit carryforwards that have no expiration date. At December 31, 2014, the Company also had foreign NOL carryforwards of approximately $3.7 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.

Approximately $36.8 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 (in thousands):

	2014	2013
NOL carryforwards	$ 168,778	$ 136,583
R&D credit carryforwards	13,668	11,227
Capitalized R&D	6,548	8,003
Stock-based compensation	6,630	3,221
Other	1,615	1,207
	197,239	160,241
Valuation allowance	(197,239)	(160,241)
	$ —	$ —

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 $37.0 million in 2014 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 2014.

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 (in thousands):

	2014	2013	2012
Amounts computed at statutory federal rate	$(31,441)	$(12,902)	$(7,088)
Stock-based compensation and other permanent differences	1,417	244	209
Reduction of deferred tax assets under Section 382 of the Code	—	2,781	—
R&D credits	(2,420)	(1,269)	(937)
Change in valuation allowance	37,106	13,509	8,375
State taxes	(5,092)	(2,140)	(1,171)
Foreign taxes	4	—	(4)
Other	426	(223)	616
	$ 0	$ 0	$ 0

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, 2014 and 2013, the Company did not have any liabilities recorded for uncertain tax positions.

10. Commitments and Contingencies

Leases

The Company leases facilities and certain equipment under noncancelable operating leases that expire at various dates through February 2019. Under the terms of the facilities leases, the Company is required to pay its proportionate share of property taxes, insurance and normal maintenance costs.

Future noncancelable minimum payment obligations under operating lease arrangements, including facilities and equipment, were as follows at December 31, 2014 (in thousands):

2015	$2,119
2016	2,021
2017	1,455
2018	1,506
2019	260
Thereafter	—
	$7,361

Rent expense for operating leases is recorded on a straight-line basis over the life of the lease term. Facility operating leases contain fixed and determinable escalation clauses. The difference between the rent expense and the rent paid is recorded as deferred rent. Rent expense under the Company's facility and equipment leases was $1.2 million, $594,000, and $663,000, for the years ended December 31, 2014, 2013, and 2012, respectively.

External Services

The Company has entered into agreements with contract research organizations and other external service providers primarily for services in connection with the development and planned commercialization of its product candidates. The Company was contractually obligated for up to approximately $16.3 million of future services under these agreements as of December 31, 2014. The nature of the work being conducted under the Company's agreements with external service providers 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.

Contingent Regulatory Milestone Payments

In connection with the Company's 2006 license agreement with the Ipsen Group, the Company may be obligated in future periods to make certain regulatory milestone payments. These milestone payments may never occur as they are contingent on the achievement of future regulatory events which may never be attained. These one-time payments include $2.5 million payable upon the successful filing of the first regulatory application with the U.S. Food and Drug Administration ("FDA") and $8.0 million payable upon obtaining the first regulatory approval from the FDA. The Company would also be required to make royalty payments of up to two percent on net product sales, if any.

11. Selected Quarterly Financial Data (Unaudited)

The following financial information reflects all normal recurring adjustments, which are, in the opinion of management, necessary for a fair statement of the results of the interim periods. Summarized quarterly data for the years ended December 31, 2014 and 2013 are as follows (in thousands, except per share data):

	Fiscal Year 2014 Quarters				
	1st	2nd	3rd	4th	Total
Revenues	$ 30	$ 28	$ 15	$ 47	$ 120
Net loss	$(17,828)	$(21,495)	$(24,786)	$(28,366)	$(92,475)
Basic and diluted net loss per share(1)	$ (0.19)	$ (0.22)	$ (0.25)	$ (0.28)	$ (0.95)

	Fiscal Year 2013 Quarters				
	1st	2nd	3rd	4th	Total
Revenues	$ 417	$ 451	$ 240	$ 37	$ 1,145
Net loss	$ (6,123)	$ (9,081)	$(10,695)	$(12,049)	$(37,948)
Basic and diluted net loss per share(1)	$ (0.08)	$ (0.11)	$ (0.12)	$ (0.13)	$ (0.44)

(1) 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.

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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, 2009 through December 31, 2014 in (i) our common stock, (ii) the NASDAQ Biotechnology Index, and (iii) the NASDAQ U.S. Benchmark TR 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).