

ACADIA PHARMACEUTICALS INC

Form 424B5

January 07, 2016

Table of Contents

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-194273

CALCULATION OF REGISTRATION FEE

TITLE OF EACH CLASS OF SECURITIES TO BE REGISTERED	AMOUNT TO BE REGISTERED(1)	PROPOSED MAXIMUM OFFERING PRICE PER UNIT	PROPOSED MAXIMUM AGGREGATE OFFERING PRICE	AMOUNT OF REGISTRATION FEE(2)
Common Stock, \$0.0001 par value per share	11,896,551	\$29.00	\$344,999,979	\$34,741.50

- (1) Includes shares of Common Stock that may be purchased by the underwriters pursuant to their option to purchase additional shares of Common Stock.
- (2) The registration fee is calculated and being paid pursuant to Rule 457(r) under the Securities Act of 1933, as amended, and relates to the Registration Statement on Form S-3 (File No. 333-194273) filed by the Registrant on March 3, 2014.

Table of Contents**PROSPECTUS SUPPLEMENT**

(To Prospectus dated March 3, 2014)

10,344,827 Shares**Common Stock**

We are selling 10,344,827 shares of our common stock.

Our common stock is listed on The NASDAQ Global Select Market under the symbol ACAD . On January 6, 2016, the last reported sale price for our common stock on The NASDAQ Global Select Market was \$29.24 per share.

Investing in our common stock involves significant risks. See Risk Factors on page S-5 of this prospectus supplement and the documents incorporated by reference into this prospectus supplement.

	Per Share	Total
Public offering price	\$29.00	\$299,999,983
Underwriting discount ⁽¹⁾	\$1.74	\$17,999,999
Proceeds, before expenses, to us	\$27.26	\$281,999,984

(1) We refer you to Underwriting beginning on page S-41 of this prospectus supplement for additional information regarding total underwriting compensation.

The underwriters may also exercise their option to purchase up to an additional 1,551,724 shares from us, at the public offering price, less the underwriting discount, for 30 days after the date of this prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved these securities or determined if this prospectus supplement or the accompanying prospectus is accurate or complete. Any representation to the contrary is a criminal offense.

Entities affiliated with Baker Bros. Advisors LP and two of our directors, Julian C. Baker and Dr. Stephen R. Biggar, have agreed to purchase approximately \$75.0 million of the shares of common stock offered in this offering at the public offering price.

The shares will be ready for delivery on or about January 12, 2016.

Joint Book-Running Managers

BofA Merrill Lynch

J.P. Morgan

Lead Manager

Cowen and Company

Co-Managers

**JMP Securities
H.C. Wainwright & Co.**

**Needham & Company
Ladenburg Thalmann**

The date of this prospectus supplement is January 6, 2016

Table of Contents

TABLE OF CONTENTS

Prospectus Supplement

	Page
<u>About this Prospectus Supplement</u>	S-ii
<u>Prospectus Supplement Summary</u>	S-1
<u>Risk Factors</u>	S-5
<u>Note Regarding Forward-Looking Statements</u>	S-38
<u>Use of Proceeds</u>	S-39
<u>Dilution</u>	S-40
<u>Underwriting</u>	S-41
<u>Legal Matters</u>	S-48
<u>Experts</u>	S-48
<u>Where You Can Find More Information</u>	S-48
<u>Incorporation of Certain Information by Reference</u>	S-48

Prospectus

	Page
<u>ACADIA Pharmaceuticals Inc.</u>	1
<u>Risk Factors</u>	1
<u>Note Regarding Forward-Looking Statements</u>	1
<u>Use of Proceeds</u>	2
<u>Plan of Distribution</u>	2
<u>Legal Matters</u>	3
<u>Experts</u>	3
<u>Where You Can Find More Information</u>	4

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering of common stock and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus dated March 3, 2014, including the documents incorporated by reference therein, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference that was filed with the Securities and Exchange Commission, or SEC, before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference in the accompanying prospectus the statement in the document having the later date modifies or supersedes the earlier statement. You should assume that the information contained in this prospectus supplement is accurate as of the date on the cover page of this prospectus supplement only and that any information we have incorporated by reference or included in the accompanying prospectus is accurate only as of the date given in the document incorporated by reference or as of the date of the prospectus, as applicable, regardless of the time of delivery of this prospectus supplement or the accompanying prospectus or any sale of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

We have not, and the underwriters have not, authorized anyone to provide you with different information than that which is contained in or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we have authorized for use in connection with this offering. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus supplement entitled **Where You Can Find More Information and **Incorporation of Certain Information by Reference**.**

Unless otherwise mentioned or unless the context requires otherwise, all references in this prospectus supplement to ACADIA , the Company , we , our or similar references mean ACADIA Pharmaceuticals Inc. together with its wholly owned subsidiaries.

This prospectus supplement, the accompanying prospectus and the information incorporated herein and therein by reference may include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus supplement or the accompanying prospectus are the property of their respective owners.

Table of Contents

PROSPECTUS SUPPLEMENT SUMMARY

*This summary highlights selected information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary does not contain all the information you should consider before investing in our common stock. You should read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including the factors described under the heading **Risk Factors** in this prospectus supplement on page S-5 and the financial and other information incorporated by reference in this prospectus supplement and the accompanying prospectus, as well as the information included in any free writing prospectus that we have authorized for use in connection with this offering, before making an investment decision.*

Company Overview

We are a biopharmaceutical company focused on the development and commercialization of innovative small molecule drugs that address unmet medical needs in 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. NUPLAZID is a selective serotonin inverse agonist, or SSIA, preferentially targeting 5-HT_{2A} receptors. Through this novel mechanism, NUPLAZID has demonstrated significant efficacy in Parkinson's disease psychosis in our Phase III pivotal trial and has the potential to avoid many of the debilitating side effects of existing antipsychotics, none of which are approved for use in PDP patients. We hold worldwide commercialization rights to pimavanserin.

We are pursuing Parkinson's disease psychosis as our lead indication for NUPLAZID. In September 2015, we submitted a New Drug Application, or NDA, to the U.S. Food and Drug Administration, or FDA, for NUPLAZID for the treatment of psychosis associated with Parkinson's disease, which was accepted for priority review by the FDA on October 30, 2015 with a Prescription Drug User Fee Act, or PDUFA, goal date of May 1, 2016. In September 2014, we announced that the FDA granted Breakthrough Therapy designation for NUPLAZID for the treatment of Parkinson's disease psychosis. The Breakthrough Therapy designation was created 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 physicians who are high prescribers of antipsychotics for PDP patients, including neurologists, psychiatrists and long-term care physicians.

Table of Contents

Our Product Candidates and Programs

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

We believe that pimavanserin has the potential to address important unmet medical needs in neurological and psychiatric disorders beyond PDP and we plan to continue to study the use of pimavanserin in multiple disease states. We believe Alzheimer's disease represents one of our most important opportunities for further exploration. We are currently conducting a Phase II study exploring the utility of pimavanserin for the treatment of Alzheimer's disease psychosis, or ADP, a disorder for which no drug is currently approved by the FDA, and expect to complete enrollment of this study in the first half of 2016 and have top-line results of the study in the second half of 2016. We also plan to initiate a Phase II study in Alzheimer's disease agitation in the first half of 2016. We believe schizophrenia also represents a disease with multiple unmet or ill-served needs and we are currently evaluating the most attractive development opportunities there. 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 are currently conducting a significant life cycle planning project to assess and prioritize other medically important and attractive development opportunities for pimavanserin.

Recent Events

In September 2015, we submitted an NDA to the FDA for NUPLAZID for the treatment of psychosis associated with Parkinson's disease. The NDA was accepted for priority review by the FDA on October 30, 2015 with a PDUFA goal date of May 1, 2016.

Our NDA submission is based on data from a comprehensive development program assessing the safety and efficacy of NUPLAZID for Parkinson's disease psychosis. The NDA includes data from the pivotal Phase III -020 Study, in which NUPLAZID met all primary and secondary endpoints with statistical significance, along with supportive data from other studies with NUPLAZID. In the -020 Study, NUPLAZID significantly reduced psychosis compared to placebo in patients with Parkinson's disease psychosis with no worsening of motor function. These results were further supported by significant improvements in all secondary efficacy measures and by significant benefits in exploratory efficacy measures of nighttime sleep, daytime wakefulness and caregiver burden. Consistent with previous studies, NUPLAZID was safe and well tolerated in the -020 Study.

Table of Contents

Corporate Information

We were originally incorporated in Vermont in 1993 as Receptor Technologies, Inc. In 1997, we reincorporated in Delaware. Our executive offices are located at 3611 Valley Centre Drive, Suite 300, San Diego, California 92130, and our telephone number is (858) 558-2871. Our website address is www.acadia-pharm.com. Information contained on our website is not a part of this prospectus supplement, the accompanying prospectus or any of the documents incorporated by reference herein.

S-3

Table of Contents

The Offering

Common stock offered by us	10,344,827 shares
Common stock to be outstanding immediately after this offering	111,241,027 shares (or 112,792,751 shares if the underwriters exercise in full their option to purchase additional shares)
Option to purchase additional shares	The underwriters have an option to purchase up to 1,551,724 additional shares of our common stock. The underwriters may exercise this option at any time within 30 days from the date of this prospectus supplement.
Use of proceeds	We intend to use the net proceeds of this offering to fund commercialization efforts for NUPLAZID, ongoing and new clinical trials and development efforts for pimavanserin, and for general corporate purposes, including working capital. See Use of Proceeds on page S-39 of this prospectus supplement.
NASDAQ Global Select Market Listing	Our common stock is listed on The NASDAQ Global Select Market under the symbol ACAD .
Risk Factors	Investing in our common stock involves a high degree of risk. See Risk Factors on page S-5 of this prospectus supplement.
The number of shares of our common stock to be outstanding immediately after this offering is based on 100,896,200 shares outstanding as of September 30, 2015, and excludes as of that date:	

10,543,320 shares of common stock issuable upon the exercise of outstanding stock options under our equity incentive plans, with a weighted average exercise price of \$20.76 per share;

6,203,901 shares of common stock available for future grants under our equity incentive plans;

350,834 shares of common stock available for issuance under our employee stock purchase plan; and

1,965,968 shares of common stock issuable upon the exercise of outstanding warrants at a weighted average exercise price of \$1.03 per share.

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise by the underwriters of their option to purchase additional shares and no exercise of outstanding stock options or warrants.

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Entities affiliated with Baker Bros. Advisors LP and two of our directors, Julian C. Baker and Dr. Stephen R. Biggar, have agreed to purchase approximately \$75.0 million of the shares of common stock offered in this offering at the public offering price.

S-4

Table of Contents**RISK FACTORS**

Investing in our common stock involves a high degree of risk. Our business, prospects, financial condition or operating results could be materially adversely affected by the risks identified below, as well as other risks not currently known to us or that we currently consider immaterial. The trading price of our common stock could decline due to any of these risks, and you may lose all or part of your investment. In assessing the risks described below, you should also refer to the information contained in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2015 and other documents which are incorporated by reference in this prospectus supplement and the accompanying prospectus in their entirety, and other documents that we file from time to time with the SEC.

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. In September 2015, we submitted our NDA for NUPLAZID for the treatment of PDP to the FDA, which was accepted for priority review by the FDA on October 30, 2015 with a Prescription Drug User Fee Act, or PDUFA, goal date of May 1, 2016. While the FDA has agreed to review our 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 the FDA's substantive review of the entire NDA to assess whether it 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 approve an NDA for NUPLAZID and there are many components to an NDA filing beyond the efficacy and safety data provided to 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. Further, we previously delayed the submission of our NDA for NUPLAZID to complete the preparation of manufacturing quality systems to support commercial manufacturing and supply of NUPLAZID, in order to support the FDA's review of the NDA, and we cannot be certain that our additional preparation of these quality systems will be sufficient to support the review of the NDA.

Even though our NDA submission was 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

S-5

Table of Contents

treatment of PDP or any other indication. In addition, neither the receipt of priority review for the NDA nor the breakthrough therapy designation increases the likelihood that our NDA will be approved. There is no guarantee that the FDA will determine that our safety and efficacy data are sufficient to support approval for NUPLAZID for PDP or that the potential benefits associated with NUPLAZID outweigh any safety concerns. The FDA or any advisory committee may not agree that the change shown on the SAPS-PD scale used to measure the primary endpoint in our -020 Study demonstrates a clinically meaningful benefit to patients. While the FDA did not object to our use of the SAPS-PD scale for the primary endpoint in the -020 study prior to our commencement of the study, this scale, which is a 9-item subset of the full 20-item SAPS scale, had never previously been used in a clinical study. In addition, the FDA may determine that our manufacturing and quality systems, or those of our third-party suppliers, or that the clinical trials conducted with NUPLAZID are not sufficient to support approval of the NDA. Additionally, as part of the FDA's review, the FDA has and will continue to provide comments and ask questions about the NDA for NUPLAZID, including questions about our pre-clinical and clinical studies and our manufacturing processes for NUPLAZID. Whether the FDA approves the NDA may depend in part on our responses to these comments and questions. If the FDA does not find our responses to its comments and questions satisfactory, it may choose not to approve the NDA for NUPLAZID. 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, therefore, 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, including a Risk Evaluation and Mitigation Strategy, or REMS, to mitigate the risk of off-label use in populations where the FDA may believe that the potential risks of NUPLAZID use may outweigh its benefits. 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 processes, 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.

S-6

Table of Contents

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. In connection with 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, select psychiatrists, and pharmacists and physicians in 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.

S-7

Table of Contents

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 at least 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.

S-8

Table of Contents

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. The current environment is putting pressure on companies to price products below what they may feel is appropriate. Selling NUPLAZID at less than an optimized price could impact our revenues and overall success as a company. 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 to 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 our Annual 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

S-9

Table of Contents

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 fees enacted under the ACA on certain drug product sales, subject to limited exceptions. It is possible that these fees, if applicable, would adversely affect our financial performance. 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.

We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, physician payment transparency laws and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

Although we do not currently have any marketed products, if we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations may be directly, or indirectly through our customers and third-party payors, subject to various U.S. federal and state healthcare laws and regulations, including, without limitation, the U.S. federal Anti-Kickback Statute, the U.S. federal False Claims Act, and physician sunshine laws and regulations. These laws may impact, among other things, our proposed sales, marketing and education programs and constrain the business or financial arrangements with healthcare providers, physicians and other parties through which we market, sell and distribute our products for which we obtain marketing approval. In addition, we may be subject to patient data privacy and security regulation by both the U.S. federal government and the states in which we conduct our business. Finally, we may be subject to additional healthcare, statutory and regulatory requirements and enforcement by foreign regulatory authorities in jurisdictions in which we conduct our business. The laws that may affect our ability to operate include:

the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration (including

S-10

Table of Contents

any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

the U.S. federal civil and criminal false claims laws and civil monetary penalties laws, including the civil False Claims Act, which impose criminal and civil penalties, through civil whistleblower or qui tam actions, on individuals or entities for, among other things, knowingly presenting, or causing to be presented to the U.S. federal government, claims for payment or approval that are false or fraudulent or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;

the U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and its implementing regulations, and as amended again by the Final HIPAA Omnibus Rule, Modifications to the HIPAA Privacy, Security, Enforcement and Breach Notification Rules Under HITECH and the Genetic Information Nondiscrimination Act; Other Modifications to the HIPAA Rules, published in January 2013, which imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by covered entities subject to the rule, such as health plans, healthcare clearinghouses and healthcare providers as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information;

the U.S. Federal Food, Drug and Cosmetic Act, or FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;

the U.S. federal physician payment transparency requirements, sometimes referred to as the Physician Payments Sunshine Act, which was enacted as part of the ACA and its implementing regulations and requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is

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available under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to the Centers for Medicare and Medicaid Services, or CMS, information related to certain payments and other transfers of value made to physicians, other healthcare providers, and teaching hospitals, as well as ownership and investment interests held by physicians and other healthcare providers and their immediate family members;

analogous state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and

S-11

Table of Contents

marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; and state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and

European and other foreign law equivalents of each of the laws, including reporting requirements detailing interactions with and payments to healthcare providers.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from U.S. government funded healthcare programs, such as Medicare and Medicaid, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits, and the curtailment or restructuring of our operations. Moreover, while we do not bill third-party payors directly and our customers make the ultimate decision on how to submit claims, from time-to-time, after approval of our product candidates, we may provide reimbursement guidance to patients and healthcare providers. If a government authority were to conclude that we provided improper advice and/or encouraged the submission of a false claim for reimbursement, we could face action against us by government authorities. If any of the physicians or other providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment. If any of the above occur, it could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of our product candidates outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

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 the product for off-label uses.

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 in the United States or for uses in other jurisdictions that differ from those approved by the 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 requirements and restrictions of 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

S-12

Table of Contents

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 FDCA, 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 September 30, 2015, we had an accumulated deficit of approximately \$616.8 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. In September 2015, we submitted our NDA for NUPLAZID for the treatment of PDP to the FDA, which was accepted for priority review by the FDA on October 30, 2015 with a PDUFA goal date of May 1, 2016. The regulatory approval process is time consuming and uncertain and there is no guarantee that our NDA for NUPLAZID will be 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 nine months ended September 30, 2015 were from reimbursement of patent costs under our agreements with third parties. The research term of our 2003 research collaboration with Allergan concluded in March 2013 and we no longer recognize revenues from this collaboration. In addition, in September 2015, Allergan provided notice of termination of our collaboration focused on muscarinic product candidates and we will not be receiving any further payments under that agreement. Thus, any payments from Allergan pursuant to our continuing collaboration in chronic pain 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 \$240.7 million at September 30, 2015. 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;

S-13

Table of Contents

the costs of preparing applications for regulatory approvals for NUPLAZID and other product candidates, as well as the costs required to support review of such applications;

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, including the costs incurred in defending against claims made in the consolidated putative class action that was commenced following our announcement of the update to the timing of our planned NDA submission to the FDA for NUPLAZID and the subsequent decline of the price of our common stock in March 2015.

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, or 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. We currently plan to submit our Marketing Authorization Application for

Table of Contents

NUPLAZID in Europe in the second quarter of 2016. Even if we obtain regulatory approval in the United States, 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 the work that we have conducted to support our NDA submission for PDP. 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. Even though we successfully completed the -020 Study, those results are not predictive of the results of any additional studies that we may undertake with pimavanserin, including any post-approval studies that we may undertake if NUPLAZID is approved for marketing by the FDA. We believe that pimavanserin also may have utility in indications other than PDP, such as Alzheimer's disease psychosis, or ADP, other indications related to Alzheimer's disease, 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 or any Alzheimer's disease indication, 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 clinical trials of pimavanserin for indications other than PDP, 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, a small group of psychiatrists, and pharmacists and physicians in long-term care facilities 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.

We are currently conducting a significant life cycle planning project for pimavanserin that was initiated in the second quarter of 2015 and through which we expect to formulate a multi-year plan to develop pimavanserin in indications

beyond PDP. Given the unique profile of pimavanserin, together with the list of potential indications we could pursue, this is a substantial and a very important undertaking. When we complete the project in the first quarter of 2016, we expect to have a long-term plan of which indications we intend to

S-15

Table of Contents

pursue for pimavanserin as we seek to maximize the opportunities for this compound. If our life-cycle planning and execution is not conducted successfully, then we may not realize the full value from pimavanserin or may devote substantial resources to develop pimavanserin for indications that are ultimately not successful or do not yield adequate returns. Furthermore, even if NUPLAZID is approved for PDP, a failure in a subsequent study for another indication could harm our ability to successfully market NUPLAZID for PDP or could lead to it being withdrawn from the market. If we are unable to develop pimavanserin for other indications, we may not be able to maximize the potential of the compound and that could have a material adverse effect on our future revenues and our success as a company.

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 submitted our NDA for NUPLAZID for PDP in September 2015 that was accepted for priority review by the FDA on October 30, 2015 with a PDUFA goal date of May 1, 2016. An unfavorable outcome in any of the ongoing or future development efforts for NUPLAZID, including any unfavorable decisions related to our NDA, 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, devote additional substantial resources to, 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 those within schizophrenia and Alzheimer's disease. We have an ongoing clinical collaboration with Allergan with separate product candidates for the treatment of chronic pain that has reached Phase II development.

In connection with clinical trials, we face risks that:

a product candidate may not prove to be efficacious or safe;

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.

S-16

Table of Contents

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

Table of Contents

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 our 1999 collaboration agreement with Allergan focused on muscarinic product candidates was terminated as of December 2015. Any additional payments from our ongoing collaboration agreement with Allergan in chronic pain are dependent upon further advancement of an applicable product candidate. Unless these milestones are met, we will not receive future revenues from our ongoing collaboration 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 March 2015, Actavis plc acquired Allergan. Then, in November 2015, Allergan announced it entered into an agreement with Pfizer Inc. under which Pfizer will acquire Allergan. Allergan also previously has announced that it was seeking a partner for further development and commercialization of drug candidates in our chronic pain program under our continuing collaboration. In connection with Actavis' acquisition of Allergan, and any related restructuring, Allergan elected to terminate our collaboration focused on muscarinic product candidates, including the glaucoma program covered by such collaboration, and, in connection with Actavis' and subsequently Pfizer's acquisition of Allergan, it may choose to devote substantially less resources to the chronic pain program or could discontinue such program 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 this program to date. In addition, Allergan can terminate our existing chronic pain collaboration upon prior notice to us, as it has done with the glaucoma collaboration. Allergan may be more likely to terminate, or decline to continue, our chronic pain collaboration in connection with Actavis' and Pfizer's acquisition of Allergan.

If Allergan elects to devote substantially less resources to the chronic pain program, 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 program. If Allergan elects to discontinue the chronic pain program and terminates our collaboration agreement, as was the case with the glaucoma program, the discontinued program may revert to us, in which case we would need to evaluate whether to continue advancing such program alone or with a new collaborator. Either advancing such program 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 have not yet made a determination with regard to any further development of the glaucoma program that will be returning to us under the collaboration focused on muscarinic product candidates.

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 and industry 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.

S-18

Table of Contents

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 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 an ongoing collaboration with Allergan for the development of product candidates related to chronic pain. Allergan may also pursue other research programs related to pain management that are independent from our collaboration in this therapeutic area. In March 2015, Actavis acquired Allergan and, in November 2015, Allergan announced it entered into an agreement with Pfizer under which Pfizer will acquire Allergan. Actavis and Pfizer may have, or acquire rights to, additional programs related to chronic pain, which could impact the strategy with respect to

the development of product candidates covered by our ongoing collaboration.

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.

S-19

Table of Contents

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.

In August 2015, we contracted with Patheon Pharmaceuticals Inc., or Patheon, to manufacture NUPLAZID drug product for commercial use in the United States following any commercial launch of NUPLAZID, if approved by the FDA. Additionally, in August 2015 we contracted with BASF Pharma (Evionnaz)

S-20

Table of Contents

SA, which was subsequently acquired by Siegfried Pharma Evionnaz SA, or Siegfried, in October 2015, to manufacture active pharmaceutical ingredient, or API, to be used in the manufacture of NUPLAZID drug product for commercial use. However, we have not entered into any agreements with any alternate suppliers for NUPLAZID drug product or NUPLAZID API. Even if we are able to enter into other 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.

Even though we entered into an agreement with Patheon for the manufacture of NUPLAZID drug product and with Siegfried for the manufacture of NUPLAZID API for commercial use, and even if we successfully enter into long-term agreements with other 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 of API and one supplier of drug product 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 manufacturers of our product candidates, including Patheon and Siegfried, 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 prior to any grant of regulatory approval by 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.

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.

S-21

Table of Contents

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, 2015, we employed approximately 160 employees. Although we have already added several capabilities, we will need to add additional 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;

S-22

Table of Contents

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.

As we grow as an organization and expand from a development to a commercial-stage company, we may make certain changes to our organization in order to properly manage our growth, which may include changes to the composition of our board of directors and management. Any such changes may be disruptive to us as an organization, which could harm our business.

As we continue to grow as an organization, including by expanding our development efforts and building out our commercial capabilities in anticipation of commercial launch of NUPLAZID, if approved, we will evaluate, and may implement, changes to our organization that may be appropriate in order to properly manage and direct our growth and transformation into a commercial-stage company. These changes may include changes to the size and composition of our management and/or board of directors, as appropriate, to include individuals with substantial experience in managing or serving on the boards of directors of commercial-stage pharmaceutical companies. For example, our board recently elected two new board members, Dr. Edmund Harrigan and Julian Baker, to replace two board members who resigned in November and December 2015. Additionally, in September 2015, we named Steve Davis, who had been serving as our Interim CEO since March 2015, to be our President and Chief Executive Officer and to be a member of our Board of Directors. We also recently named Dr. Serge Stankovic as our new Executive Vice President, Head of Research and Development, to replace our previous Executive Vice President, Development and Chief Medical Officer who resigned in November 2015. We currently are recruiting for a new Chief Financial Officer and may decide to hire other executive level employees as we grow. Any such significant changes to the organization may distract management or otherwise be disruptive to us as a company, which could harm our business.

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

S-23

Table of Contents

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;

S-24

Table of Contents

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, including the costs incurred in defending against claims made in the two putative class action complaints, which have now been consolidated into one action, filed following our March 2015 announcement of the update to the timing of our planned NDA submission to the FDA for NUPLAZID and the subsequent decline of the price of our common stock; 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.

Future changes to U.S. and non-U.S. tax laws could materially adversely affect us.

During the first half of 2015, we licensed worldwide intellectual property rights related to pimavanserin in certain indications to ACADIA Pharmaceuticals GmbH, our wholly-owned Swiss subsidiary. Our goals for the establishment of ACADIA Pharmaceuticals GmbH, and the licensing of worldwide intellectual property rights for pimavanserin, include building a platform for long-term operational and financial efficiencies, including tax-related efficiencies. Future changes in U.S. and non-U.S. tax laws, including implementation of international tax reform relating to the tax treatment of multinational corporations, if enacted, may reduce or eliminate any potential financial efficiencies that we hope to achieve by establishing this operational structure. Additionally, taxing authorities, such as the U.S. Internal Revenue Service, may audit and otherwise challenge these types of arrangements, and have done so with other companies in the pharmaceutical industry. If any such changes in tax law are enacted, or our licensing of worldwide intellectual property rights for pimavanserin to our Swiss subsidiary is otherwise challenged, this could materially adversely affect our business.

S-25

Table of Contents

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.

S-26

Table of Contents

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

S-27

Table of Contents

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

S-28

Table of Contents

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.

Central provisions of The Leahy-Smith America Invents Act, or the America Invents Act went into effect on September 16, 2012 and on March 16, 2013. The America Invents Act includes a number of significant changes to U.S. patent law. These changes include provisions that affect the way patent applications are being filed, prosecuted and litigated. For example, the America Invents Act enacted proceedings involving post-issuance patent review procedures, such as inter partes review, or IPR, and post-grant review, that allow third parties to challenge the validity of an issued patent in front of the United States PTO Patent Trial and Appeal Board. Each proceeding has different eligibility criteria and different patentability challenges that can be raised. IPRs permit any person (except a party who has been litigating the patent for more than a year) to challenge the validity of the patent on the grounds that it was anticipated or made obvious by prior art. Patents covering pharmaceutical products have been subject to attack in IPRs from generic drug companies and from hedge funds. 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

S-29

Table of Contents

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, or 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

S-30

Table of Contents

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

S-31

Table of Contents

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.

S-32

Table of Contents

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;

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;

S-33

Table of Contents

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. For example, in March 2015, following our announcement of the update to the timing of our planned NDA submission to the FDA for NUPLAZID for the treatment of PDP and the subsequent decline of the price of our common stock, two putative securities class action complaints were filed against us and certain of our current and former officers, which complaints were subsequently consolidated into one complaint. The complaint generally alleges that the defendants violated Sections 10(b) and 20(a)

of the Securities Exchange Act of 1934 by making materially false and misleading statements regarding the timing of our planned NDA submission to the FDA for NUPLAZID, thereby artificially inflating the price of our common stock. If we are not successful in defense of these claims, we may have to make significant payments to, or other settlements with, our stockholders and their attorneys. Even if such claims are not successful, the litigation could result in substantial costs and divert our management's attention and resources, which could have a material adverse effect on our business, operating results or financial condition.

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

Table of Contents

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 two of our directors, Julian C. Baker and Dr. Stephen R. Biggar, which we refer to as the Baker Entities. In connection with this offering of common stock, we entered into a formal registration rights agreement with the Baker Entities to provide for these rights. Based on information available to us, the Baker Entities collectively beneficially owned approximately 20.3% of our common stock as of September 30, 2015. Under the registration rights agreement we have agreed that, if at any time and from time to time after the expiration of an initial period of approximately 90 days, the Baker Entities demand that we register their shares of our common stock for resale under the Securities Act, we would be obligated to effect such registration. Our registration obligations under this registration rights agreement cover all shares now held or hereafter acquired (including any shares acquired in this offering) by the Baker Entities, will be in effect for up to ten years, and include our obligation to facilitate certain underwritten public offerings of our common stock by the Baker Entities in the future. If the Baker Entities, by exercising these registration and/or underwriting rights or otherwise, sell a large number of our shares, or the market perceives that the Baker Entities intend to sell a large number of our shares, this could adversely affect the market price of our common stock. 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;

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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;

S-35

Table of Contents

establish advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings;

prohibit our stockholders from making certain changes to our amended and restated certificate of incorporation or amended and restated bylaws except with 66 ²/₃ 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.

Risks Related to This Offering

Management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. Our failure to apply these funds effectively could have a material adverse effect on our business, delay the development of our product candidates, including pimavanserin, and cause the price of our common stock to decline.

If you purchase the common stock sold in this offering, you will experience immediate and substantial dilution in your investment. You will experience further dilution if we issue additional equity securities in future fundraising transactions.

Since the price per share of our common stock being offered is substantially higher than the net tangible book value per share of our common stock, you will suffer substantial dilution with respect to the net tangible book value of the common stock you purchase in this offering. Based on the public offering price of \$29.00 per share and our net

tangible book value as of September 30, 2015, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of \$24.43 per share with respect to the net tangible

S-36

Table of Contents

book value of the common stock. See the section entitled "Dilution" for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering.

In addition, we have a significant number of stock options and warrants outstanding. To the extent that outstanding stock options or warrants have been or may be exercised or other shares issued, investors purchasing our common stock in this offering may experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders or result in downward pressure on the price of our common stock.