ACADIA PHARMACEUTICALS INC
Form S-3ASR
November 26, 2018
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As filed with the Securities and Exchange Commission on November 26, 2018

Registration No. 333-

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM S-3

REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

ACADIA PHARMACEUTICALS INC.

(Exact name of Registrant as specified in its charter)

Delaware	**06-1376651**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification Number)**

3611 Valley Centre Drive, Suite 300

San Diego, CA 92130

(858) 558-2871

(Address, including zip code, and telephone number, including area code, of registrant s principal executive offices)

Stephen R. Davis

Chief Executive Officer

ACADIA Pharmaceuticals Inc.

3611 Valley Centre Drive, Suite 300, San Diego, CA 92130

(858) 558-2871

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Austin D. Kim
Executive Vice President, General Counsel & Secretary
ACADIA Pharmaceuticals Inc.
3611 Valley Centre Drive, Suite 300
San Diego, CA 92130
(858) 558-2871

L. Kay Chandler
Sean M. Clayton
Cooley LLP
4401 Eastgate Mall
San Diego, CA 92121
(858) 550-6000

Approximate date of commencement of proposed sale to the public:

From time to time after this Registration Statement becomes effective.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box:

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box:

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering:

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering:

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box:

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box:

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company.

Large accelerated filer	Accelerated filer
Non-accelerated filer	Smaller reporting company
	Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

CALCULATION OF REGISTRATION FEE

Title of Each Class of	**Amount**	**Proposed Maximum**	**Proposed Maximum**	**Amount of**

Securities to be Registered	Amount to be Registered	Proposed Maximum Offering Price Per Unit	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee
Common Stock, $0.0001 par value per share	(1)	(1)	(1)	(2)

(1) Omitted pursuant to Form S-3 General Instruction II.E. Such indeterminate number or amount of common stock is being registered as may from time to time be offered at indeterminate prices.
(2) In accordance with Rules 456(b) and 457(r), the registrant is deferring payment of all of the registration fee.

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PROSPECTUS

Common Stock

We may, from time to time, offer to sell common stock in amounts, at prices and on terms described in one or more supplements to this prospectus. You should read this prospectus and any supplement carefully before you invest.

This prospectus describes some of the general terms that may apply to an offering of our common stock. The specific terms and any other information relating to a specific offering will be set forth in a post-effective amendment to the registration statement of which this prospectus is a part or in a supplement to this prospectus or may be set forth in one or more documents incorporated by reference in this prospectus. The amendment or supplement, as applicable, may also add, update or change information contained in this prospectus with respect to that specific offering.

Our common stock may be offered and sold in the same offering or in separate offerings; to or through underwriters, dealers, and agents; or directly to purchasers; or through a combination of these methods. The names of any underwriter, dealer or agents involved in the sale of our common stock and their compensation will be described in an applicable prospectus supplement. See Plan of Distribution .

Our common stock is listed on The Nasdaq Global Select Market under the symbol ACAD . On November 23, 2018, the last reported sale price for our common stock was $18.51. You are encouraged to obtain current market quotations for shares of our common stock.

Our principal executive offices are located at 3611 Valley Centre Drive, Suite 300, San Diego, California 92130, and our telephone number at that address is (858) 558-2871.

Investing in our common stock involves a high degree of risk. See Risk Factors on page 3 of this prospectus.

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

The date of this prospectus is November 26, 2018.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the SEC, using the shelf registration process as a well-known seasoned issuer, as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act. By using a shelf registration statement, we may offer and sell from time to time in one or more offerings the common stock described in this prospectus. No limit exists on the aggregate number of shares of common stock we may sell pursuant to the registration statement.

This prospectus provides you with a general description of our common stock. Each time we sell shares of our common stock, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement, or information incorporated by reference in this prospectus or any prospectus supplement that is of a more recent date, may also add, update or change information contained in this prospectus. To the extent that any statement that we make in a prospectus supplement is inconsistent with statements made in this prospectus, the statements made in this prospectus will be deemed modified or superseded by those made in the prospectus supplement. You should read both this prospectus and any applicable prospectus supplement, together with the additional information described below under the heading Where You Can Find More Information . This prospectus may not be used to consummate a sale of our common stock unless it is accompanied by a prospectus supplement. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to an offering of our common stock.

We have not authorized anyone to provide you with information other than the information contained or incorporated by reference in this prospectus and any related prospectus supplement, or in any free writing prospectus that we may authorize in connection with an offering of our shares of common stock. No one is making offers to sell or seeking offers to buy shares of our common stock in any jurisdiction where the offer or sale is not permitted. You should assume that the information contained in this prospectus and any prospectus supplement is accurate only as of the date on the front of this prospectus or the prospectus supplement, as applicable, and that any information we have incorporated by reference in this prospectus or any prospectus supplement is accurate only as of the date given in the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any sale of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

References in this prospectus to ACADIA , the Company , we , us and our refer to ACADIA Pharmaceuticals Inc. together with our wholly-owned subsidiaries.

ACADIA and NUPLAZID are our registered trademarks. Our logos and trademarks are the property of ACADIA Pharmaceuticals Inc. All other brand names or trademarks appearing in this prospectus are the property of their

respective holders. Use or display by us of other parties trademarks, trade dress, or products in this prospectus is not intended to, and does not, imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owners.

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ACADIA PHARMACEUTICALS INC.

We are a biopharmaceutical company focused on the development and commercialization of innovative medicines to address unmet medical needs in central nervous system disorders. We have a portfolio of product opportunities led by our novel drug, NUPLAZID (pimavanserin), which was approved by the U.S. Food and Drug Administration, or FDA, in April 2016 for the treatment of hallucinations and delusions associated with Parkinson s disease psychosis, or PD Psychosis, and is the only drug approved in the United States for this condition. NUPLAZID is a selective serotonin inverse agonist, or SSIA, preferentially targeting 5- HT_{2A} receptors. Through this novel mechanism, NUPLAZID demonstrated significant efficacy in reducing the hallucinations and delusions associated with PD Psychosis in our Phase 3 pivotal trial and has the potential to avoid many of the debilitating side effects of existing antipsychotics, none of which are approved by the FDA for the treatment of PD Psychosis. We hold worldwide commercialization rights to pimavanserin. We launched NUPLAZID in the United States in May 2016 with the recommended dosing of 34 mg once a day taken as two 17 mg tablets. In June 2018, the FDA approved a 34 mg NUPLAZID capsule formulation that provides patients with the recommended 34 mg once daily dose in a single, small capsule, reducing patient pill burden versus the previous administration of two 17 mg tablets. In addition, the FDA approved a 10 mg NUPLAZID tablet that provides an optimized lower dosage strength in those patients who are concomitantly receiving strong cytochrome 3A4 inhibitors which can inhibit the metabolism of NUPLAZID.

We believe that pimavanserin has the potential to address important unmet medical needs in neurological and psychiatric disorders in addition to PD Psychosis and we plan to continue to study the use of pimavanserin in multiple disease states. For example, we believe dementia-related psychosis represents one of our most important opportunities for further exploration. In December 2016, we announced positive top-line results from our Phase 2 study exploring the utility of pimavanserin for the treatment of Alzheimer s disease psychosis, or AD Psychosis, a disorder for which no drug is currently approved by the FDA. Following our End-of-Phase 2 Meeting with the FDA and agreement with the agency on our clinical development plan, we initiated our Phase 3 HARMONY relapse prevention study in the fourth quarter of 2017, which allows us to evaluate pimavanserin for a broader indication than AD Psychosis alone. More specifically, HARMONY will evaluate pimavanserin for the treatment of hallucinations and delusions associated with dementia-related psychosis, which includes psychosis in patients with Alzheimer s disease, dementia with Lewy bodies, Parkinson s disease dementia, vascular dementia and frontotemporal dementia. Furthermore, in the fourth quarter of 2017, the FDA granted Breakthrough Therapy Designation to pimavanserin for this dementia-related psychosis indication.

We also believe schizophrenia represents a disease with multiple unmet needs and we are currently exploring the utility of pimavanserin in this area. Despite a large number of FDA-approved therapies for schizophrenia, current drugs do not adequately address some very important symptoms of schizophrenia, such as the inadequate response to current antipsychotic treatment of psychotic symptoms and negative symptoms. In the fourth quarter of 2016, we initiated two studies evaluating the adjunctive use of pimavanserin in patients with schizophrenia. ENHANCE-1 is a Phase 3 study evaluating pimavanserin for adjunctive treatment of schizophrenia in patients with an inadequate response to their current antipsychotic therapy. We expect to report top-line results of the ENHANCE-1 study mid-2019. ADVANCE is a Phase 2 study evaluating pimavanserin for adjunctive treatment in patients with negative symptoms of schizophrenia.

According to the National Institute of Mental Health, major depressive disorder (MDD) affects approximately 16 million adults in the United States, with approximately 2.5 million adults treated with adjunctive therapy. The majority of people who suffer from MDD do not respond adequately to initial antidepressant therapy. In October 2018, we announced positive top-line results from CLARITY, a Phase 2 study evaluating pimavanserin for adjunctive treatment in 207 patients with MDD who had a confirmed inadequate response to existing first-line, SSRI or SNRI, antidepressant therapy. In the study, pimavanserin met the pre-specified primary and key secondary endpoints with

statistical significance and positive results were also observed in seven additional secondary endpoints including response rate, improvement in sexual function, and a reduction in daytime sleepiness. Pimavanserin was generally well-tolerated in the study with no meaningful

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weight gain observed or impact on motor function. We plan to meet with the FDA and initiate two Phase 3 clinical trials in adjunctive MDD in first half of 2019.

In August 2018, we acquired an exclusive North American license to develop and commercialize trofinetide for Rett syndrome and other indications from Neuren Pharmaceuticals. Rett syndrome is a debilitating neurological disorder that occurs in females following apparently normal development for the first six months of life. Typically, between six to eighteen months of age, patients experience a period of rapid decline with loss of purposeful hand use and spoken communication and inability to independently conduct activities of daily living. Symptoms also include seizures, disorganized breathing patterns, scoliosis and sleep disturbances. Trofinetide is a novel synthetic analog of the amino-terminal tripeptide of IGF-1 designed to treat the core symptoms of Rett syndrome by reducing neuroinflammation and supporting synaptic function. Trofinetide has been granted FDA Fast Track Status and Orphan Drug Designation in the U.S. and Europe for the treatment of Rett syndrome. Currently, there are no approved medicines for the treatment of Rett syndrome. We plan to initiate a Phase 3 randomized, double-blind placebo-controlled study evaluating trofinetide in girls with Rett syndrome in the second half of 2019.

We were incorporated in Delaware in January 1997. Our principal executive offices are located at 3611 Valley Centre Drive, Suite 300, San Diego, California 92130, and our telephone number at that address is (858) 558-2871. Our website address is www.acadia-pharm.com. The information contained in, or that can be accessed through, our website is not part of this prospectus.

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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, 2018 and other documents which are incorporated by reference in this 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 successful commercialization of NUPLAZID, which received approval in April 2016 from the U.S. Food and Drug Administration, or FDA, as a treatment for hallucinations and delusions associated with Parkinson s disease psychosis, and became available for prescription in the United States in May 2016. To the extent 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.

NUPLAZID is our only drug that has been approved for sale and it has only been approved for the treatment of hallucinations and delusions associated with Parkinson s disease psychosis, or PD Psychosis, in the United States. We are focusing a significant portion of our activities and resources on NUPLAZID, and we believe our prospects are highly dependent on, and a significant portion of the value of our company relates to, our ability to successfully commercialize NUPLAZID in the United States.

Successful commercialization of NUPLAZID is subject to many risks. Prior to NUPLAZID, we had never, as an organization, launched or commercialized any product, and there is no guarantee that we will be able to successfully commercialize NUPLAZID for its approved indication. There are numerous examples of failures to meet high expectations of market potential, including by pharmaceutical companies with more experience and resources than us. While we have established our commercial team and have hired our U.S. sales force, we will need to refine and further develop the team in order to successfully commercialize NUPLAZID. Even if we are successful in developing our commercial team, there are many factors that could cause the commercialization of NUPLAZID to be unsuccessful, including a number of factors that are outside our control. Because no drug has previously been approved by the FDA for the treatment of hallucinations and delusions associated with PD Psychosis, it is especially difficult to estimate NUPLAZID s market potential. The commercial success of NUPLAZID depends on the extent to which patients and physicians recognize and diagnose PD Psychosis and accept and adopt NUPLAZID as a treatment for hallucinations and delusions associated with PD Psychosis, and we do not know whether our or others estimates in this regard will be accurate. For example, if the patient population suffering from hallucinations and delusions associated with PD Psychosis is smaller than we estimate or if physicians are unwilling to prescribe or patients are unwilling to take NUPLAZID due to its boxed warning, perceived safety issues or for other reasons, the commercial potential of NUPLAZID will be limited. We have limited information about how physicians, patients and payors have responded and will respond to the pricing of NUPLAZID. We have changed, and may continue to change, the price of NUPLAZID from time to time. Physicians may not prescribe NUPLAZID and patients may be unwilling to use NUPLAZID if coverage is not provided or reimbursement is inadequate to cover a significant portion of the cost. Additionally, any negative publicity related to NUPLAZID or negative development for NUPLAZID in our post-marketing commitments, in clinical development in additional indications, or in regulatory processes in other jurisdictions, may adversely impact the commercial results and potential of NUPLAZID. Thus, significant uncertainty remains regarding the commercial potential of NUPLAZID.

If the commercialization of NUPLAZID is unsuccessful or perceived as disappointing, our stock price could decline significantly and the long-term success of the product and our company could be harmed.

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If we do not obtain regulatory approval of NUPLAZID for other indications in the United States, or for any indication in foreign jurisdictions, we will not be able to market NUPLAZID for other indications or in other jurisdictions, which will limit our commercial revenues.

While NUPLAZID (pimavanserin) has been approved by the FDA for the treatment of hallucinations and delusions associated with PD Psychosis, it has not been approved by the FDA for any other indications, and it has not been approved in any other jurisdiction for this indication or for any other indication. In order to market NUPLAZID for other indications or in other jurisdictions, we must obtain regulatory approval for each of those indications and in each of the applicable jurisdictions, and we may never be able to obtain such approval. Approval of NUPLAZID by the FDA for the treatment of hallucinations and delusions associated with PD Psychosis does not ensure that foreign jurisdictions will also approve NUPLAZID for that indication, nor does it ensure that NUPLAZID will be approved by the FDA for any other indication. In the fourth quarter of 2016, we initiated clinical studies of pimavanserin in schizophrenia and depression and, in the fourth quarter of 2017, we initiated a Phase 3 study of pimavanserin in dementia-related psychosis, an indication for which no drug has been approved. There is no guarantee that any of these studies will be successful, or that the FDA or any regulatory authority in foreign jurisdictions will approve NUPLAZID for any of those indications. The research, testing, manufacturing, labeling, approval, sale, import, export, marketing, and distribution of pharmaceutical product candidates are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, whose regulations differ from country to country. 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 for other indications or in other jurisdictions. This will require additional time, expertise and expense, including the potential need to conduct additional studies or development work for other jurisdictions beyond the work that we have conducted to support our NDA submission in PD Psychosis. In addition, strategic considerations need to be taken into account when determining whether and when to submit NUPLAZID for approval in other jurisdictions. For example, in the fourth quarter of 2016, the European Medicines Agency, or EMA, approved our proposed pediatric investigation plan related to our planned submission of a marketing authorization application, or MAA, for NUPLAZID in Europe. However, in light of our continuing clinical development of pimavanserin in indications other than in PD Psychosis, and the time-limited data exclusivity currently granted by the EMA that commences on first approval of a product in Europe, we deferred submission of the MAA and we do not yet have a revised estimate of when we will make that filing. If we do not receive marketing approval for NUPLAZID for any other indication or from any regulatory agency outside of the United States, we will never be able to commercialize NUPLAZID for any other indication in the United States or for any indication in any other jurisdiction. Even if we do receive additional regulatory approvals, we may not be successful in commercializing those opportunities.

If the results or timing of regulatory filings, the regulatory process, regulatory developments, clinical trials or preclinical studies, or other activities, actions or decisions related to NUPLAZID do not meet our or others expectations, the market price of our common stock could decline significantly.

Even though the FDA has granted approval of NUPLAZID for the treatment of hallucinations and delusions associated with PD Psychosis, the terms of the approval may limit its commercial potential. Additionally, NUPLAZID is still subject to substantial, ongoing regulatory requirements.

Even though the FDA has granted approval of NUPLAZID, the scope and terms of the approval may limit our ability to commercialize NUPLAZID and, therefore, our ability to generate substantial sales revenues. The FDA has approved NUPLAZID only for the treatment of hallucinations and delusions associated with PD Psychosis. The label for NUPLAZID also contains a boxed warning that elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death, and that NUPLAZID is not approved for the treatment of patients

with dementia-related psychosis unrelated to the hallucinations and delusions associated with PD Psychosis.

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Additionally, NUPLAZID is approved only for the treatment of hallucinations and delusions associated with PD Psychosis, rather than for the treatment of PD Psychosis and/or other symptoms of PD Psychosis, which may cause confusion for prescribing physicians. This confusion could result in physicians not prescribing NUPLAZID for patients diagnosed with PD Psychosis. In addition, the boxed warning may discourage physicians from prescribing NUPLAZID to patients diagnosed with PD Psychosis, including those with dementia.

In connection with the FDA approval, we committed to conduct the following post-marketing studies: (i) a randomized, placebo-controlled withdrawal study in PD Psychosis patients treated with NUPLAZID, (ii) studies to collect additional data to add to the NUPLAZID safety database from an aggregate of at least 500 predominantly frail and elderly subjects on NUPLAZID in one or more randomized, placebo-controlled studies of eight or more weeks duration, (iii) a drug-drug interaction study with NUPLAZID and a strong CYP3A4 inducer, and (iv) re-analysis of tissue samples from certain previously conducted pre-clinical studies. We have completed the re-analysis of tissue samples but the remaining studies are ongoing. If we fail to comply with our remaining post-marketing commitments, or if the results of the post-marketing studies, or any other ongoing or planned clinical studies of NUPLAZID, are negative, the FDA could decide to withdraw approval, add warnings or narrow the approved indication in the product label.

The manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for NUPLAZID will also continue to 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 council for harmonization guidelines and good laboratory practices, which are regulations and guidelines enforced by the FDA for all of our nonclinical and clinical development and for any clinical trials that we conduct post- approval.

Discovery of any issues post-approval, including any safety concerns, such as unexpected side effects or drug-drug interaction problems, adverse events of unanticipated severity or frequency, or concerns over misuse or abuse of the product, problems with the facilities where the product is manufactured, packaged or distributed, or failure to comply with regulatory requirements, may result in, among other things, restrictions on NUPLAZID or on us, including:

- withdrawal of approval, addition of warnings or narrowing of the approved indication in the product label;
- requirement of a Risk Evaluation and Mitigation Strategy to mitigate the risk of off-label use in populations where the FDA may believe that the potential risks of use may outweigh its benefits;
- voluntary or mandatory recalls;
- warning letters;
- suspension of any ongoing clinical studies;

refusal by the FDA or other regulatory authorities to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of product approvals;

restrictions on operations, including restrictions on the marketing or manufacturing of the product or the imposition of costly new manufacturing requirements; or

seizure or detention, or refusal to permit the import or export of products.

If any of these actions were to occur, we may have to discontinue the commercialization of NUPLAZID, limit our sales and marketing efforts, conduct further post-approval studies, and/or discontinue or change any other ongoing or planned clinical studies, which in turn could result in significant expense and delay or limit our ability to generate sales revenues.

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NUPLAZID has only been studied in a limited number of patients and in limited populations. As we continue to commercialize NUPLAZID, it is becoming available to a much larger number of patients and in broader populations, and we do not know whether the results of NUPLAZID use in such larger number of patients and broader populations will be consistent with the results from our clinical studies.

Prior to commencing our commercial launch of NUPLAZID in May 2016, NUPLAZID was administered only to a limited number of patients and in limited populations in clinical studies, including our successful pivotal -020 Phase 3 trial with NUPLAZID for the treatment of PD Psychosis, or the -020 Study. While the FDA granted approval of NUPLAZID based on the data included in the NDA, including data from the -020 Study, we do not know whether the results when a large number of patients and broader populations are exposed to NUPLAZID, including results related to safety and efficacy, will be consistent with the results from earlier clinical studies of NUPLAZID that served as the basis for the approval of NUPLAZID. New data relating to NUPLAZID, including from adverse event reports and post-marketing studies in the United States, and from other ongoing clinical studies, may result in changes to the product label and may adversely affect sales, or result in withdrawal of NUPLAZID from the market. The FDA and regulatory authorities in other jurisdictions may also consider the new data in reviewing NUPLAZID marketing applications for indications other than in PD Psychosis and/or in other jurisdictions, or impose additional post-approval requirements. If any of these actions were to occur, it could result in significant expense and delay or limit our ability to generate sales revenues.

We currently have very limited experience as a company in marketing and distributing pharmaceutical products and rely on a limited network of third-party distributors and pharmacies to distribute NUPLAZID. If we are unable to effectively commercialize NUPLAZID, we may not be able to generate adequate product revenues.

NUPLAZID is our only drug that has been approved for sale by any regulatory body, and it became available for prescription in the United States in May 2016. As such, we currently have limited experience commercializing pharmaceutical products as an organization. In order to successfully market NUPLAZID, we must continue to develop our sales, marketing, managerial, compliance, and related capabilities or make arrangements with third parties to perform these services. If we are unable to maintain and develop adequate sales, marketing, and distribution capabilities, whether independently or with third parties, we may not be able to appropriately commercialize NUPLAZID and may not become profitable.

We employ our own internal specialty sales force to commercialize NUPLAZID for the treatment of PD Psychosis as part of our commercialization strategy in the United States. We will need to refine and further develop our sales force as we continue our commercialization efforts, and we will be competing with other pharmaceutical and biotechnology companies to recruit, hire, train and retain marketing and sales personnel. These efforts will continue to be expensive and time-consuming, and we cannot be certain that we will be able to successfully refine and further develop our sales force.

Additionally, our strategy in the United States includes distributing NUPLAZID solely through a limited network of third-party specialty distributors and specialty pharmacies. While we have entered into agreements with each of these distributors and pharmacies to distribute NUPLAZID in the United States, they may not perform as agreed or they may terminate their agreements with us. Also, we may need to enter into agreements with additional distributors or pharmacies, and there is no guarantee that we will be able to do so on commercially reasonable terms or at all. If we are unable to maintain and, if needed, expand, our network of specialty distributors and specialty pharmacies, we would be exposed to substantial distribution risk.

In the event we are unable to effectively develop and maintain our commercial team, including our U.S. sales force, or maintain and, if needed, expand, our network of specialty distributors and specialty pharmacies, our ability to

effectively commercialize NUPLAZID and generate product revenues would be limited.

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

Prior to its launch in May 2016, none of the members of our sales force had ever promoted NUPLAZID. In addition, NUPLAZID is the first drug approved by the FDA for the treatment of hallucinations and delusions associated with PD Psychosis. As a result, we are and will continue to be required to expend significant time and resources to train our sales force to be credible, persuasive, and compliant with applicable laws in marketing NUPLAZID for the treatment of hallucinations and delusions associated with PD Psychosis to neurologists, select psychiatrists, and pharmacists and physicians in long-term care facilities. In addition, we must ensure that consistent and appropriate messages about NUPLAZID are being delivered to our potential customers by our sales force. If we are unable to effectively train our sales force and equip them with effective materials, including medical and sales literature to help them inform and educate potential customers about the benefits of NUPLAZID and its proper administration, our efforts to successfully commercialize NUPLAZID could be put in jeopardy, which would negatively impact our ability to generate product revenues.

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

The degree of market acceptance by physicians, healthcare professionals and third-party payors of NUPLAZID, and any other product for which we obtain regulatory approval, and our profitability and growth, will depend on a number of factors, including:

the ability to provide acceptable evidence of safety and efficacy;

the scope of the approved indication(s) for the product;

the inclusion of any warnings or contraindications in the product label;

the relative convenience and ease of administration;

the prevalence and severity of any adverse side effects;

the 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 will not generate sufficient revenues to achieve or maintain profitability.

With respect to NUPLAZID specifically, 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 is available to treat hallucinations and delusions associated with PD Psychosis, an indication for which no other FDA-approved pharmaceutical treatment currently exists. Because of this, it is particularly difficult to estimate NUPLAZID s market potential and how physicians, payors and patients will respond to changes in the price of NUPLAZID. 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 PD Psychosis, the rate of diagnosis of PD Psychosis, the prevalence and rate of hallucinations and delusions in patients diagnosed with PD Psychosis, the rate of physician adoption of NUPLAZID, the potential impact of payor restrictions regarding 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 PD Psychosis to

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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 PD Psychosis. For these reasons, even if PD Psychosis occurs in high rates among patients with Parkinson s disease, it may be underdiagnosed. Even if PD Psychosis is diagnosed, physicians may not prescribe treatment for hallucinations and delusions associated with PD Psychosis, and if they do prescribe treatment, they may prescribe other drugs, even though they are not approved in PD Psychosis, instead of NUPLAZID. Additionally, NUPLAZID is approved only for the treatment of hallucinations and delusions associated with PD Psychosis, rather than for the treatment of PD Psychosis and/or other symptoms of PD Psychosis, which may cause confusion for prescribing physicians. This confusion could result in physicians not prescribing NUPLAZID for patients diagnosed with PD Psychosis. In addition, even if NUPLAZID is prescribed for the treatment of hallucinations and delusions associated with PD Psychosis, issues may arise with respect to patient adherence and compliance rates. For example, the current recommended dosing of NUPLAZID is 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. The FDA has approved our NDA for a 34 mg capsule for NUPLAZID to, among other things, try to mitigate this risk. The 34 mg capsule is now commercially available. We also submitted a supplemental NDA, or sNDA, for a 10 mg tablet to the FDA, which was also approved and is now commercially available. The 10 mg tablet provides an optimized lower dosage strength in those patients who are concomitantly receiving strong cytochrome 3A4 inhibitors which can inhibit the metabolism of NUPLAZID. Both the 34 mg and the 10 mg doses are intended to be taken once a day. Patients may elect, whether at the direction of their physician or otherwise, to not adhere to the recommended dosing, which could result in far lower efficacy for the 10 mg and 34 mg doses. 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 label for NUPLAZID also contains a boxed warning that elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death, and that NUPLAZID is not approved for the treatment of patients with dementia-related psychosis unrelated to the hallucinations and delusions associated with PD Psychosis. There has also been recent attention to publicly reported deaths of patients that were prescribed NUPLAZID, and the FDA conducted an evaluation of available information about NUPLAZID. On September 20, 2018 the U.S. FDA issued a statement concluding: The U.S. FDA has completed a review of all post marketing reports of deaths and serious adverse events (SAEs) reported with the use of NUPLAZID. Based on an analysis of all available data, FDA did not identify any new or unexpected safety findings with NUPLAZID, or findings that are inconsistent with the established safety profile currently described in the drug label. After a thorough review, FDA s conclusion remains unchanged that the drug s benefits outweigh its risks for patients with hallucinations and delusions of Parkinson s disease psychosis. Regardless, perceptions that NUPLAZID is unsafe, even if unfounded, may discourage physicians from prescribing or patients from taking NUPLAZID.

Thus, 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 prescribing behaviors and market adoption.

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 have unacceptably high co-pay amounts.

Patients who are prescribed medicine for the treatment of their conditions generally rely on third-party payors, including governmental healthcare programs, such as Medicare and Medicaid, managed care organizations and commercial payors, among others, to reimburse all or part of the costs associated with their prescription drugs. Coverage and adequate reimbursement from third-party commercial payors is critical to product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor drug products when lower cost therapeutic

alternatives are already available or subsequently become available. Even

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with 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 its cost.

In addition, the market for NUPLAZID depends 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 alternative is available, even if not approved for the indication for which NUPLAZID is approved.

In many foreign countries, particularly the countries of the European Union, the pricing of prescription drugs is subject to government control. In some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. We may face competition from lower-priced products in foreign countries that have placed price controls on pharmaceutical products. In addition, there may be importation of foreign products that compete with NUPLAZID, and any other products we may market, which could negatively impact our profitability.

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. We have changed, and may continue to change, the price of NUPLAZID from time to time, however, we do not know if the price we have selected, or may select in the future, for NUPLAZID is or will be the optimized price. Additionally, we do not know whether and to what extent third-party payors will react to any possible future changes in the price of NUPLAZID. In the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Further, one payor s determination to provide coverage and reimbursement for a product does not assure that other payors also will provide coverage and reimbursement for the product. Therefore, coverage and reimbursement for NUPLAZID may 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 NUPLAZID 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.

Healthcare reform measures may negatively impact our ability to sell NUPLAZID or our product candidates, if approved, profitably.

In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory proposals to change the healthcare system in ways that could impact our ability to sell NUPLAZID, and any other potential products, as described in greater detail in the Government Regulation section of our Annual Report on Form 10-K for the year ended December 31, 2017. 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, additional reporting requirements and/or oversight, and the curtailment or 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

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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.

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. With respect to pharmaceutical products, the ACA, among other things, expanded and increased industry rebates for drugs covered by Medicaid and made changes to the coverage requirements under Medicare Part D, Medicare s prescription drug benefits program. Some of the provisions of the ACA have yet to be implemented, and there have been legal and political challenges to certain aspects of the ACA, as well as recent efforts by the Trump administration to repeal and replace certain aspects of the ACA, and we expect such challenges to continue. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been enacted. The Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the individual mandate . Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain fees mandated by the ACA, including the so-called Cadillac tax on certain high cost employer-sponsored insurance plans and the annual fee imposed on certain health insurance providers based on market share. Further, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the donut hole , and also increases in 2019 the percentage that a drug manufacturer must discount the cost of prescription drugs from 50 percent under current law to 70 percent. Given that the current patient population for NUPLAZID is primarily Medicare beneficiaries, accelerating the closure of the coverage gap and the increase in the discount that must be paid, could have a significant impact on the Company s business in 2019 and beyond. More recently, in July 2018, CMS announced that it is suspending further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program pending the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. Congress could consider additional legislation to repeal or repeal and replace other elements of the ACA. At this time, the ultimate content, timing or effect of any healthcare reform legislation on the U.S. healthcare industry and its impact to our business is unclear.

An expansion in the government s role in the U.S. healthcare industry may increase existing congressional or governmental agency scrutiny on price increases, such as the ones we have implemented for NUPLAZID, cause general downward pressure on the prices of prescription drug products, lower reimbursements for providers using NUPLAZID or any other product for which we obtain regulatory approval, reduce product utilization and adversely affect our business and results of operations. There have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for drugs. For example, the Trump administration s budget proposal for fiscal year 2019 contains additional drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid and to eliminate cost sharing for generic drugs for low-income patients. The Trump

administration also released a Blueprint , or plan, to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug

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manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. The Department of Health and Human Services, or HHS, has already started the process of soliciting feedback on some of these measures and, at the same, is immediately implementing others under its existing authority. While some proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. The implementation of cost-containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize NUPLAZID or any other products for which we may receive regulatory approval.

We are subject, directly and indirectly, to federal, state and foreign healthcare laws and regulations, including 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.

Our operations are directly, and 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 sales, marketing, grants, charitable donations, and education programs and constrain the business or financial arrangements with healthcare providers, physicians, charitable foundations that support Parkinson s disease patients generally, and other parties that have the ability to directly or indirectly influence the prescribing, ordering, marketing, or distribution of our products for which we obtain marketing approval. In addition, we are 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 any kickback, bribe, or certain rebates), 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, including 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

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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 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, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;

analogous state and local 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 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; state and local 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/or the registration of pharmaceutical sales and medical representatives; 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, and the European General Data Protection

Regulation, or GDPR, which became effective in May 2018 and contains new provisions specifically directed at the processing of health information, higher sanctions and extra-territoriality measures intended to bring non-EU companies under the regulation, including companies like us that conduct clinical trials in the EU; we anticipate that over time we may expand our business operations to include additional operations in the EU and with such expansion, we would be subject to increased governmental regulation in the EU countries in which we might operate, including the GDPR.

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

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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. For example, contributions to third-party charitable foundations are a current area of significant governmental and congressional scrutiny, and we could face action if a federal or state governmental authority were to conclude that our charitable contributions to foundations that support Parkinson s disease patients generally are not compliant. 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, additional reporting requirements and/or oversight, 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, for NUPLAZID, and any other product candidates that may be approved, 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 NUPLAZID, or any other product candidates that may be approved, outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs in the United States, we could be subject to additional reimbursement requirements, fines, sanctions and exposure under other laws which could have a material adverse effect on our business, results of operations and financial condition.

We participate in the Medicaid Drug Rebate Program, as administered by CMS, and other federal and state government pricing programs in the United States, and we may participate in additional government pricing programs in the future. These programs generally require us to pay rebates or otherwise provide discounts to government payors in connection with drugs that are dispensed to beneficiaries/recipients of these programs. In some cases, such as with the Medicaid Drug Rebate Program, the rebates are based on pricing that we report on a monthly and quarterly basis to the government agencies that administer the programs. Pricing requirements and rebate/discount calculations are complex, vary among products and programs, and are often subject to interpretation by governmental or regulatory agencies and the courts. The requirements of these programs, including, by way of example, their respective terms and scope, change frequently. Responding to current and future changes may increase our costs, and the complexity of compliance will be time consuming. Invoicing for rebates is provided in arrears, and there is frequently a time lag of up to several months between the sales to which rebate notices relate and our receipt of those notices, which further complicates our ability to accurately estimate and accrue for rebates related to the Medicaid program as implemented by individual states. Thus, there can be no assurance that we will be able to identify all factors that may cause our discount and rebate payment obligations to vary from period to period, and our actual results may differ significantly from our estimated allowances for discounts and rebates. Changes in estimates and assumptions may have a material adverse effect on our business, results of operations and financial condition.

In addition, the Office of Inspector General of the Department of Health and Human Services and other Congressional, enforcement and administrative bodies have recently increased their focus on pricing requirements for products, including, but not limited to the methodologies used by manufacturers to calculate average manufacturer price, or AMP, and best price, or BP, for compliance with reporting requirements under the Medicaid Drug Rebate Program. We are liable for errors associated with our submission of pricing data and for any overcharging of

government payors. For example, failure to submit monthly/quarterly AMP and BP data on

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a timely basis could result in a civil monetary penalty of $18,107 per day for each day the submission is late beyond the due date. Failure to make necessary disclosures and/or to identify overpayments could result in allegations against us under the Federal False Claims Act and other laws and regulations. Any required refunds to the U.S. government or responding to a government investigation or enforcement action would be expensive and time consuming and could have a material adverse effect on our business, results of operations and financial condition. In addition, in the event that the CMS were to terminate our rebate agreement, no federal payments would be available under Medicaid or Medicare for our covered outpatient drugs.

The FDA granted marketing approval of NUPLAZID for the treatment of hallucinations and delusions associated with PD Psychosis, and we could face liability if a regulatory authority determines that we are promoting NUPLAZID for any 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 or patient population 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. We intend to comply with the requirements and restrictions of the FDA and other regulatory agencies with respect to our promotion of NUPLAZID, and any other products we may market, 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, or DOJ, and various U.S. Attorneys Offices, the Office of Inspector General of the Department of Health and Human Services, the FDA, the Federal Trade Commission and various state Attorneys General offices. These investigations have alleged violations of various U.S. federal and state laws and regulations, including claims asserting antitrust violations, violations of the 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, DOJ, or any other governmental agency initiates an enforcement action against us, including as a result of the civil investigative demand mentioned below, 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. In September 2018, we received a civil investigative demand, or CID, from the DOJ pursuant to the Federal False Claims Act requesting certain documents and information related to our sales and marketing of NUPLAZID. We are cooperating with the DOJ s request. Responding to the CID will require considerable resources and no assurance can be given as to the timing or outcome of the DOJ s investigation.

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, 2018, we had an accumulated deficit of approximately $1.4 billion. We expect to incur net losses over the next few years as we invest in the commercialization of NUPLAZID and advance our development programs.

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Even though we began commercializing NUPLAZID in the United States in May 2016, we still expect to incur significant expenses and net losses for at least the next few years as we continue our commercialization efforts for NUPLAZID and pursue the further development of NUPLAZID and our product candidates. Substantially all of our revenues since May 2016 were from net product sales of NUPLAZID.

We expect that our near-term revenues will be substantially dependent on our ability to generate net product sales of NUPLAZID. To the extent that we cannot generate significant revenues from the sale of NUPLAZID to cover our expenses, including the significant expenses associated with commercializing NUPLAZID and continuing to develop pimavanserin in additional indications, we may never achieve profitability and/or may have to reduce our commercialization and/or research and development activities to become profitable, which would harm our future growth prospects. Additionally, to obtain revenues from product candidates other than NUPLAZID, we must succeed, either alone or with others, in developing, obtaining regulatory approval for, manufacturing and marketing compounds with significant market potential. We may never succeed in these activities and may never generate revenues from our commercialization of NUPLAZID, or from other product candidates that may be approved, 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 continue the development and commercialization of NUPLAZID or successfully develop and commercialize our product candidates.

We have consumed substantial amounts of capital since our inception. Our cash, cash equivalents, and investment securities totaled $214.1 million at September 30, 2018. While we believe that our existing cash resources will be sufficient to fund our cash requirements through at least the next twelve months, 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, post-marketing studies for NUPLAZID to be conducted over the next several years, ongoing and planned commercial activities for NUPLAZID, and other research and development programs;
- the costs of maintaining and developing our sales and marketing capabilities for NUPLAZID;
- the costs of establishing, or contracting for, sales and marketing capabilities for other product candidates;
- the amount of U.S. product sales from NUPLAZID;
- the costs of preparing applications for regulatory approvals for NUPLAZID in jurisdictions other than the United States, and potentially in additional indications other than in PD Psychosis, and for other product candidates, as well as the costs required to support review of such applications;
- the costs of manufacturing and distributing NUPLAZID for commercial use in the United States;

our ability to obtain regulatory approval for, and subsequently generate product sales from, NUPLAZID in jurisdictions other than the United States or in additional indications other than in PD Psychosis, or from 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 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;

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- the costs involved in filing, prosecuting, enforcing, and defending patent claims and other intellectual property rights;

- the costs of maintaining or securing manufacturing arrangements and supply for clinical or commercial production of pimavanserin or other product candidates; and

- the costs associated with litigation, including the costs incurred in defending against any product liability claims that may be brought against us related to NUPLAZID.

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.

The pivotal Phase 3 study with NUPLAZID for PD Psychosis, the results of which were announced in November 2012, was our first successful pivotal Phase 3 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 the -020 Study. Additionally, in December 2016, we announced positive top-line results from our Phase 2 exploratory study of pimavanserin in patients with AD Psychosis. Even though we successfully completed this Phase 2 exploratory study, or the -019 Study, and the -020 Study, those results are not predictive of the results of any additional studies that we are currently undertaking or may undertake in the future with pimavanserin, including the post-marketing studies we committed to conduct in connection with FDA approval of NUPLAZID and the ongoing studies of pimavanserin in various indications. We believe that pimavanserin also may have utility in indications other than in PD Psychosis, such as in dementia-related psychosis, schizophrenia, and depression. However, prior to the efficacy study that we initiated in the fourth quarter of 2017, we had never tested pimavanserin in clinical studies where the primary outcome was for the broad indication of dementia-related psychosis, and prior to the study in major depressive disorder that we initiated in the fourth quarter of 2016, we had never tested pimavanserin in clinical studies in depression. Additionally, prior to the studies in schizophrenia that we initiated in the fourth quarter of 2016, we had only conducted a Phase 2 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 have the same level of success with pimavanserin in dementia-related psychosis or in other indications that we had with the -019 Study. Further, there is no guarantee that we will be successful at all in ongoing or future studies for additional indications or in our post-marketing studies, or that future results of studies of NUPLAZID for treatment in PD Psychosis or for other indications, including dementia-related psychosis, will be consistent with those from the -019 Study or -020 Study.

If we do not successfully complete additional development of NUPLAZID, we will be unable to market and sell NUPLAZID or products derived from it for indications other than the treatment of hallucinations and delusions associated with PD Psychosis, or to generate related product revenues.

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We do not have a partner for the development of pimavanserin, and are solely responsible for the advancement of this program and 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 in PD Psychosis, in the future we would need to add resources and raise additional funds in order to take this product candidate to market for indications other than in PD Psychosis or in jurisdictions outside the United States, and to conduct the necessary sales and marketing activities, and to conduct further development activities, if we do not secure a partner. Our current strategy is to commercialize NUPLAZID for the treatment of hallucinations and delusions associated with PD Psychosis in the United States using our specialty sales force focused primarily on neurologists, a small group of psychiatrists, and pharmacists and physicians in long-term care facilities who treat PD Psychosis patients. In addition, if we are approved to commercialize NUPLAZID in 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 conducted, and continue to revisit, our life-cycle planning project for pimavanserin that was initiated in 2015 and through which we have formulated a multi-year plan to develop pimavanserin in additional indications other than in PD Psychosis, including in dementia-related psychosis, schizophrenia and depression, as described above. Given the unique profile of pimavanserin, together with the list of potential indications we could pursue, this has been a substantial and important undertaking. Our life-cycle planning process will be ongoing as we evaluate appropriate indications for pimavanserin to pursue 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 though NUPLAZID is approved for the treatment of hallucinations and delusions associated with PD Psychosis, a failure in a subsequent study for another indication, including our ongoing studies in dementia-related psychosis, schizophrenia and depression, or a failure in our post-marketing studies could harm our ability to successfully market NUPLAZID for the treatment of hallucinations and delusions associated with PD Psychosis 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.

Pimavanserin is currently in development for several additional indications other than in PD Psychosis, and we are initiating the development of trofinetide for Rett syndrome. Drug development is a long, expensive and unpredictable process with 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 had an unsuccessful Phase 3 trial with NUPLAZID in 2009. An unfavorable outcome in any of our ongoing or future development efforts or in the post-marketing studies for NUPLAZID could be a major set-back for the program and for us, generally. In particular, an unfavorable outcome in our NUPLAZID

program or in the post-marketing studies 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 the fourth quarter of 2017, we initiated a Phase 3 study of

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pimavanserin in patients with dementia-related psychosis, and in the fourth quarter of 2016 we initiated both a Phase 2 and a Phase 3 study of pimavanserin as an adjunctive treatment in patients with schizophrenia as well as a Phase 2 study of pimavanserin as an adjunctive treatment in patients with major depressive disorder. We may plan and conduct additional studies in other indications in the future, and plan to initiate a Phase 3 study of trofinetide in Rett syndrome in the second half of 2019.

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.

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 recruitment, 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:

competition for internal and external resources, including clinical sites and study patients, that we may choose to allocate to other programs;

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;

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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;

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 previously have depended, and in the future may 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.

In the past, we have selectively entered into collaboration agreements with third parties. We relied on our collaborators for financial resources and for development, regulatory, and commercialization expertise for selected product candidates and we had limited control over the amount and timing of resources that our collaborators devoted to our product candidates. We may choose to rely on collaborations in the future for certain portions of our pimavanserin program or other product candidates, or for the commercialization of NUPLAZID in certain territories outside of the United States.

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.

We also face competition in our search for new collaborators, if we seek a new partner for our pimavanserin program or other programs. Given the current economic 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.

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;

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- 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 past 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. Any collaborations we establish in the future may have the effect of limiting the areas of research that we may pursue, either alone or with others. Conversely, the terms of any collaboration we may establish in the future might not restrict our collaborators from developing, 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 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. We rely on contract research organizations, medical institutions, clinical investigators, and contract laboratories to perform data collection and analysis and other aspects of our clinical trials. In addition, we also rely on third parties to assist with our preclinical studies, including studies regarding biological activity, safety, absorption, metabolism, and excretion of product candidates.

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

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

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

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

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

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fewer are approved for marketing. We cannot assure you that, even if clinical trials are completed, either we or our collaborators will submit applications for required authorizations to manufacture and/or market potential products or that any such application will be reviewed and approved by the appropriate regulatory authorities in a timely manner, if at all. Even if we or our collaborators successfully complete the clinical trials of product candidates and apply for such required authorizations, 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 in the future will continue to depend, on third parties to manufacture NUPLAZID and our product candidates. If these manufacturers fail to provide us or 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 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, NUPLAZID and our product candidates.

We have contracted with Patheon Pharmaceuticals Inc. and Catalent Pharma Solutions, LLC to manufacture NUPLAZID drug product for commercial use in the United States. Additionally, we have contracted with Siegfried AG 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 face delays or increased costs in our supply chain that could jeopardize the commercialization of NUPLAZID. Additionally, if any of our product candidates in addition to NUPLAZID are approved by the FDA or other regulatory agencies for commercial sale, or if NUPLAZID is approved for commercial sale in jurisdictions outside the United States, we will need to contract with a third party to manufacture such products for commercial sale in the United States and/or in such other jurisdictions.

Even though we have agreements with Patheon and Catalent 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 for each form of drug product (tablet and capsule) 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, maintain or obtain, as applicable, regulatory approval for or market NUPLAZID or any of our product candidates. While we believe that there will be alternative sources available to manufacture NUPLAZID and our product candidates, 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 NUPLAZID and our product candidates, including Catalent, Patheon and Siegfried, are obliged to operate in accordance with FDA-mandated current good manufacturing practices, or cGMPs, and

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we have limited 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 NUPLAZID and 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, or result in issues maintaining regulatory approval of NUPLAZID and any other product candidate that receives regulatory approval, negatively impact our commercialization of NUPLAZID, or lead to significant delays in the launch and commercialization of any other products we may have in the future. 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. 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 NUPLAZID or our product candidates 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 NUPLAZID and any other approved products will result in the loss of potential revenues and could adversely affect our ability to gain market acceptance for these products. In addition, any delay or interruption in the supply of clinical trial supplies could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely.

Failures or difficulties faced at any level of our supply chain could materially adversely affect our business and delay or impede the development and commercialization of NUPLAZID or our 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 commercialize our products, including NUPLAZID, or develop our product candidates, including pimavanserin for indications beyond PD Psychosis.

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. We are currently hiring, and in the future we expect to need to continue to hire, additional personnel as we expand our research and development efforts for pimavanserin and commercial activities for NUPLAZID. 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

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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 our commercialization efforts for NUPLAZID and the achievement of our research and development objectives.

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 September 30, 2018, we employed approximately 410 employees. Although we have already added several capabilities, we will need to add additional qualified personnel and resources. Our current infrastructure may be inadequate to support our development and commercialization efforts and expected growth. 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 NUPLAZID and any other product candidates that receive regulatory approval and to compete effectively will depend, in part, on our ability to manage any future growth effectively. In particular, as we commercialize NUPLAZID, we will need to support the training and ongoing activities of our sales force 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;
- develop our 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 as 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 capabilities for the ongoing commercialization of NUPLAZID, we have implemented, and will continue to evaluate and may implement additional, changes to our organization that may be appropriate in order to properly manage and direct our growth as 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, during 2015 and 2016, five long-standing board members either resigned from the board or did not stand for re-election, and during approximately the same timeframe our board elected three new

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board members. We hired a new head of Regulatory Affairs in February 2017 and, in March 2017, we hired a new Chief Commercial Officer following the retirement of our prior chief commercial officer. In September 2018, we hired a new head of Medical Affairs and a new Chief Scientific Officer and head of External Innovation, both of which are newly-created roles. In addition, in October 2018, our Chief Financial Officer left ACADIA for another healthcare company. We 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 we are unable to add additional commercial products to our portfolio, we may not be able to successfully leverage our commercial organization that we have assembled for the marketing and sale of NUPLAZID.

The process of integrating any acquired business, technology, service, or product may result in unforeseen operating difficulties and expenditures and may divert significant management attention from our ongoing business operations. As a result, we will incur a variety of costs in connection with an acquisition and may never realize its anticipated benefits. Moreover, any product candidate we identify, select and acquire or license may require additional, time-consuming development or regulatory efforts prior to commercial sale, including preclinical studies, if applicable, and extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to the risk of failure that is inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and/or effective for approval by regulatory authorities. In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace or be more effective or desired than other commercially available alternatives.

In addition, if we fail to successfully commercialize and further develop NUPLAZID or our 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.

If we fail to comply with the obligations in agreements under which we license intellectual property rights from third parties, we could lose license rights to certain of our product candidates.

In August 2018, we entered into a license agreement with Neuren Pharmaceuticals Limited, or Neuren, and obtained exclusive North American rights to develop and commercialize trofinetide for Rett syndrome and other indications, and we may enter into additional license agreements in the future.

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Our agreement with Neuren imposes, and we expect that future agreements where we in-license intellectual property will impose, various development, regulatory and/or commercial diligence obligations, payment of milestones and/or royalties and other obligations. If we fail to comply with our obligations under these agreements, or we are subject to bankruptcy-related proceedings, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license.

Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patents and other rights to third parties;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations;
- our right to transfer or assign the license; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may not be able to successfully develop and commercialize the related product candidates, which would have a material adverse effect on our business.

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

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

- the success of our commercialization of NUPLAZID in the United States for the treatment of hallucinations and delusions associated with PD Psychosis;
- the status and cost of our post-marketing commitments for NUPLAZID;

the variation in our gross-to-net adjustments from quarter to quarter, primarily because of the fluctuation in our share of the donut hole for Medicare Part D patients;

the status and cost of development and commercialization of pimavanserin for indications other than in PD Psychosis and in jurisdictions other than the United States;

the status and cost of development and commercialization of our 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;

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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 any product liability claims that may be brought against us related to NUPLAZID; 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.

The recently passed comprehensive tax reform bill could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law new legislation that significantly revises the Internal Revenue Code of 1986, as amended, or the Code. The newly enacted federal income tax law, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35 percent to a flat rate of 21 percent, limitation of the tax deduction for interest expense to 30 percent of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80 percent of current-year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits (including reducing the business tax credit for certain clinical testing expenses incurred in the testing of certain drugs for rare diseases or conditions). Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain if and to what extent various states will conform to the newly enacted federal tax law.

Our ability to use net operating losses to offset future taxable income may be subject to limitations.

Our net operating loss carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the newly enacted federal income tax law, federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited. It is uncertain if and to what extent various states will conform to the newly enacted federal tax law. In addition, under Section 382 of

the Code and corresponding provisions of state law, if a corporation undergoes an ownership change, which is generally defined as a greater than 50 percent change, by value, in its equity ownership over a three-year period, the corporation s ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. We have experienced ownership changes in the past and we may experience additional ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. If an ownership change occurs and our ability to use our net operating loss carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations.

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

During 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

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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. For example, we have been evaluating the impact of the December 2017 U.S. tax law changes on our current structure and future plans and may decide to make changes based on that evaluation.

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.

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. 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.

Changes or modifications in financial accounting standards, including those related to revenue recognition may harm our results of operations.

From time to time, the Financial Accounting Standards Board, or FASB, either alone or jointly with other organizations, promulgates new accounting principles that could have an adverse impact on our financial

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position, results of operations or reported cash flows. In May 2014, the FASB issued Accounting Standards Update (ASU) No. 2014-09, *Revenue from Contracts with Customers (Topic 606)*, or ASU 2014-09, which supersedes nearly all existing revenue recognition guidance under generally accepted accounting principles. ASU 2014-09 is a comprehensive new revenue recognition model that requires an entity to recognize revenue to depict the transfer of goods or services to a customer at an amount that reflects the consideration it expects to receive in exchange for those goods or services. ASU 2014-09 also requires additional disclosures about the nature, amount, timing, and uncertainty of revenue and cash flows arising from customer contracts. We adopted this new standard for the year beginning January 1, 2018 and have elected to apply the new standard using the modified retrospective method. The cumulative effect of initially applying the new revenue standard was not material and therefore, there was no adjustment to the opening balance of retained earnings. We do not expect a material impact on our net income on an ongoing basis however, any difficulties in implementing this standard, or in adopting or implementing any other new accounting standard, and to update or modify our internal controls as needed on a timely basis, could result in our failure to meet our financial reporting obligations, which could result in regulatory discipline and harm investors confidence in us. Finally, if we were to change our critical accounting estimates, including those related to the recognition of product or collaboration revenue, our operating results could be significantly affected.

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

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

Risks Related to Our Intellectual Property

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

Our commercial success depends on obtaining and maintaining intellectual property rights to our products and 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 contracts requiring confidentiality and nondisclosure.

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;

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- 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 Leahy-Smith America Invents Act, or the America Invents Act, introduced new procedures for challenging pending patent applications and issued patents; and
- technology that we may in-license may become important to some aspects of our business, however, we generally would not control the patent prosecution, maintenance or enforcement of any such in-licensed technology.

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

We regularly conduct searches to identify patents or patent applications that may prevent us from obtaining patent protection for our proprietary compounds or that could limit the rights we have claimed in our patents and patent applications. Disputes may arise regarding the ownership or inventorship of our inventions. For applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third-party or instituted by the United States Patent and Trademark Office, or United States PTO, to determine who was the first to invent the invention at issue. It is difficult to determine how such disputes would be resolved.

Applications containing a claim not entitled to priority before March 16, 2013, are not subject to interference proceedings due the change brought by the America Invents Act 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

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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 may 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, nondisclosure, and intellectual property assignment agreements with our corporate partners, employees, consultants, outside scientific collaborators, sponsored researchers, and other advisors. These agreements generally require that the other party keep confidential and not disclose to third parties all confidential information developed by the party or made known to the party by us during the course of the party s relationship with us. These agreements also generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us. Enforcing a claim that a party illegally obtained and is using our trade secrets is difficult, expensive and time consuming and the outcome is unpredictable. In addition, courts outside the United States may be less willing to protect trade secrets. We also have not entered into any noncompete agreements with any of our employees. Although each of our employees is required to sign a confidentiality agreement with us at the time of hire, we cannot guarantee that the confidential nature of our proprietary information will be maintained in the course of future employment with any of our competitors. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results and financial condition.

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

There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including post-issuance review proceedings before the United States PTO or oppositions and other comparable proceedings in foreign jurisdictions.

Central provisions of 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

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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. As another example, unlike in district court litigation, there is no presumption of validity for an issued patent, and thus, a challenger s burden to prove invalidity is by a preponderance of the evidence, as opposed to the heightened clear and convincing evidence standard. As a result of these rules and others, statistics released by the United States PTO show a high percentage of claims being invalidated in post-issuance proceedings. Moreover, with few exceptions, there is no standing requirement to petition the United States PTO for inter partes review or post-grant review. In other words, companies that have not been charged with infringement or that lack commercial interest in the patented subject matter can still petition the United States PTO for review of an issued patent. Thus, even where we have issued patents, our rights under those patents may be challenged and ultimately not provide us with sufficient protection against competitive products or processes.

While we are not currently subject to any pending intellectual property litigation or patent challenges, and are not aware of any such threatened litigation or patent challenges, we may be exposed to future litigation by third parties based on claims that our product candidates, technologies or activities infringe the intellectual property rights of others. In particular, there are many patents relating to specific genes, nucleic acids, polypeptides or the uses thereof to identify product candidates. Some of these may encompass genes or polypeptides that we utilize in our drug development activities. If our drug development activities are found to infringe any such patents, and such patents are held to be valid and enforceable, we may have to pay significant damages or seek licenses to such patents. A patentee could prevent us from using the patented genes or polypeptides for the identification or development of drug compounds. There are also many patents relating to chemical compounds and the uses thereof. If our compounds are found to infringe any such patents, and such patents are held to be valid and enforceable, we may have to pay significant damages or seek licenses to such patents. A patentee could prevent us from making, using or selling the patented compounds.

We may need to resort to litigation to enforce a patent issued to us, protect our trade secrets or determine the scope and validity of third-party proprietary rights. From time to time, we may hire scientific personnel formerly employed by other companies involved in one or more areas similar to the activities conducted by us. Either we or these individuals may be subject to allegations of trade secret misappropriation or other similar claims as a result of their prior affiliations. If we become involved in litigation, it could consume a substantial portion of our managerial and financial resources, regardless of whether we win or lose. We may not be able to afford the costs of litigation. Any legal action against us or our collaborators could lead to:

- payment of damages, which could potentially be trebled if we are found to have willfully infringed a party s patent rights;

- injunctive or other equitable relief that may effectively block our ability to further develop, commercialize, and sell products; or

we or our collaborators having to enter into license arrangements that may not be available on commercially acceptable terms, 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

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compromised by disclosure during this type of litigation. In addition, during the course of this kind of litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the trading price of our common stock.

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

The strength of patents in the pharmaceutical and biotechnology field can be highly uncertain and involve complex legal and factual questions. For example, some of our patent applications may cover the uses of gene sequences. The patentability of gene sequences and the use of gene sequences has been seriously undermined by recent decisions of the United States Supreme Court. The United States PTO s interpretation of the Supreme Court s decisions and the standards for patentability it sets forth are uncertain and could change in the future. Consequently, the issuance and scope of patents cannot be predicted with certainty. Patents, if issued, may be challenged, invalidated or circumvented. U.S. patents and patent applications may also be subject to interference proceedings as mentioned above, and U.S. patents may be subject to reexamination and post-issuance proceedings in the United States PTO (and foreign patents may be subject to opposition or comparable proceedings in the corresponding foreign patent office), which proceedings could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. Similarly, opposition or invalidity proceedings could result in loss of rights or reduction in the scope of one or more claims of a patent in foreign jurisdictions. In addition, such interference, reexamination, post-issuance and opposition proceedings may be costly. Accordingly, rights under any issued patents may not provide us with sufficient protection against competitive products or processes.

In addition, changes in or different interpretations of patent laws in the United States and foreign countries may permit others to use our discoveries or to develop and commercialize our technology and products without providing any compensation to us or may limit the number of patents or claims we can obtain. In particular, there have been proposals to shorten the exclusivity periods available under U.S. patent law that, if adopted, could substantially harm our business. The product candidates that we are developing are protected by intellectual property rights, including patents and patent applications. If any of our product candidates becomes a marketable product, we will rely on our exclusivity under patents to sell the compound and recoup our investments in the research and development of the compound. If the exclusivity period for patents is shortened, then our ability to generate revenues without competition will be reduced and our business could be materially adversely impacted. The laws of some countries do not protect intellectual property rights to the same extent as U.S. laws and those countries may lack adequate rules and procedures for defending our intellectual property rights. For example, some countries, including many in Europe, do not grant patent claims directed to methods of treating humans and, in these countries, patent protection may not be available at all to protect our product candidates. In addition, U.S. patent laws may change which could prevent or limit us from filing patent applications or patent claims to protect our products and/or technologies or limit the exclusivity periods that are available to patent holders. For example, the America Invents Act (2012) included a number of significant changes to U.S. patent law. These included changes to transition from a first-to-invent system to a first-to-file system and to the way issued patents are challenged. These changes may favor larger and more established companies that have more resources to devote to patent application filing and prosecution. It is still not clear what, if any, impact the America Invents Act will ultimately have on the cost of prosecuting our patent applications, our ability to obtain patents based on our discoveries and our ability to enforce or defend our issued patents.

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

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Risks Related to Our Industry

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

The pharmaceutical industry is subject to stringent regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Neither we nor our collaborators can market a pharmaceutical product, 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, the FDA and other regulatory agencies may impose significant restrictions on the indicated uses, conditions for use, labeling, advertising, promotion, and/or marketing of such products, and requirements for post-approval studies, including additional research and development and clinical trials. These limitations may limit the size of the market for the product or result in the incurrence of additional costs. Any delay or failure in obtaining required approvals could have a material adverse effect on our ability to generate revenues from the particular product candidate.

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

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

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

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

For example, the use of NUPLAZID for the treatment of hallucinations and delusions associated with PD Psychosis competes with off-label use of antipsychotic drugs, including the generic drugs quetiapine and clozapine. If approved, pimavanserin for the treatment of dementia-related psychosis would compete with off-label use of antipsychotic drugs, including the generic drugs risperidone and quetiapine, 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. Pimavanserin for the adjunctive treatment of schizophrenia, if approved for that indication, would compete with Rexulti, marketed by Otsuka Pharmaceutical Co., Ltd., Latuda, marketed by Sunovion Pharmaceuticals Inc., and generic drugs, including olanzapine, risperidone, aripiprazole and clozapine. Pimavanserin for the adjunctive treatment of major depressive

disorder, if approved for that indication, would compete with Rexulti, off-label use of antipsychotic drugs and the generic drugs olanzapine, risperidone, aripiprazole and clozapine. 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.

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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;
- obtaining FDA and other regulatory approvals; and
- commercializing pharmaceutical products.

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.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of NUPLAZID or any other product for which we obtain regulatory approval, or development or commercialization of our product candidates.

We face an inherent risk of product liability as a result of the commercial sales of NUPLAZID in the United States and the clinical testing of our product candidates, and will face an even greater risk following commercial launch of NUPLAZID in additional jurisdictions, if approved, or if we engage in the clinical testing of new product candidates or commercialize any additional products. For example, we may be sued if NUPLAZID or any other product we develop allegedly causes injury or is found to be otherwise unsuitable for administration in humans. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our products or product candidates that we may develop;

injury to our reputation;

withdrawal of clinical trial participants;

initiation of investigations by regulators;

costs to defend the related litigation;

a diversion of management s time and our resources;

substantial monetary awards to trial participants or patients;

product recalls, withdrawals or labeling, marketing or promotional restrictions;

loss of revenue;

exhaustion of any available insurance and our capital resources;

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the inability to commercialize our products or product candidates; and

a decline in our stock price.

Although we currently have product liability insurance that covers our clinical trials and the commercialization of NUPLAZID, we may need to increase and expand this coverage, including if we commence larger scale trials and if other 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. If we determine that it is prudent to increase our product liability coverage, we may be unable to obtain such increased coverage on acceptable terms or at all. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. Our liability could exceed our total assets if we do not prevail in a lawsuit from any injury caused by our drug products. Product liability claims could have a material adverse effect on our business and results of operations.

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 success of our commercialization of NUPLAZID in the United States for the treatment of hallucinations and delusions associated with PD Psychosis;

the status and cost of our post-marketing commitments for NUPLAZID;

the status and cost of development and commercialization of pimavanserin for indications other than in PD Psychosis and in jurisdictions other than the United States;

the status and cost of development and commercialization of our 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;

any other communications or guidance from the FDA or other regulatory authorities that pertain to NUPLAZID or our product candidates;

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;

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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 PD Psychosis 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 alleged 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. The parties agreed to a settlement in that case, which was approved by the court in January 2018. Additionally, between July 19 and August 3, 2018, following the recent negative publicity about NUPLAZID, three putative securities class action complaints were filed against us and certain of our current executive officers. The complaints generally allege that defendants violated Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 by making materially false and misleading statements regarding our business, operations, and prospects by failing to disclose that adverse events and safety concerns regarding NUPLAZID threatened initial and continuing FDA approval, and by failing to disclose that we engaged in business practices likely to attract regulatory scrutiny. 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 significantly reduce the market price of our common stock. 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 our January 2016 public offering of common stock, we entered into a formal registration rights agreement with the Baker Entities to provide for these rights. Under the registration rights agreement we have agreed that, if at any time and from time to time, 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. On April 1, 2016, we filed a registration statement covering the sale of up to 26,179,806 shares of our common stock, which includes 500,000 shares of our common stock issuable upon the exercise of warrants that were owned by the Baker Entities as of September 30, 2018, and which represent approximately 21 percent of our outstanding shares. Our registration obligations under this registration rights agreement cover all shares now held or later acquired by the Baker Entities will be in effect for up to 10 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 sell a large number of our shares, or the market perceives that the

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Baker Entities intend to sell a large number of our shares, this could adversely affect the market price of our common stock. We also may elect to sell an indeterminate number of shares on our own behalf pursuant to a 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 our interests or the interests of other stockholders and they may act in a manner that advances their best interests and not necessarily those of our other stockholders.

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

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

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

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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.

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NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains, and the documents incorporated by reference herein and any applicable prospectus supplement may contain, forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements may include, but are not limited to statements about:

- the benefits to be derived from NUPLAZID (pimavanserin) and from our drug candidates, including trofinetide;
- the potential market opportunities for pimavanserin and our drug candidates;
- our strategy for the commercialization of NUPLAZID;
- our plans for exploring and developing pimavanserin for indications other than Parkinson s disease psychosis and trofinetide for Rett syndrome;
- our plans and timing with respect to seeking regulatory approvals;
- the potential commercialization of any of our drug candidates that receive regulatory approval;
- the progress, timing, results or implications of clinical trials and other development activities involving NUPLAZID and our drug candidates;
- our strategy for discovering, developing and, if approved, commercializing drug candidates;
- our existing and potential future collaborations;
- our estimates of future payments, revenues and profitability;
- our estimates regarding our capital requirements, future expenses and need for additional financing;

possible changes in legislation; and

our use of the proceeds from any offerings under this prospectus.

In some cases, you can identify forward-looking statements by terms such as may , will , should , could , would , plans , anticipates , believes , estimates , projects , predicts , potential and similar expressions (including their negative) intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss many of these risks in greater detail under the heading Risk Factors in our SEC filings, and may provide additional information in any applicable prospectus supplement. Also, these forward-looking statements represent our estimates and assumptions only as of the date of the document containing the applicable statement.

You should read this prospectus, the registration statement of which this prospectus is a part, the documents incorporated by reference herein, and any applicable prospectus supplement completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements. Unless required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. Thus, you should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements.

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USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds from the sale of our common stock offered under this prospectus. Unless we indicate otherwise in the applicable prospectus supplement, we anticipate that any net proceeds will be used for working capital and general corporate purposes. We will set forth in the applicable prospectus supplement our intended use for the net proceeds received from the sale of any common stock sold pursuant to that prospectus supplement.

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PLAN OF DISTRIBUTION

We may sell the common stock to one or more underwriters for public offering and sale by them and may also sell the common stock to investors directly or through agents. We will name any underwriter or agent involved in the offer and sale of common stock in the applicable prospectus supplement. We have reserved the right to sell or exchange our common stock directly to investors on our own behalf in those jurisdictions where we are authorized to do so.

We may distribute the common stock from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

We may also, from time to time, authorize dealers, acting as our agents, to offer and sell the common stock upon the terms and conditions set forth in the applicable prospectus supplement. We, or the purchasers of the common stock for whom the underwriters may act as agents, may compensate underwriters in the form of underwriting discounts or commissions, in connection with the sale of the common stock. Underwriters may sell the common stock to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for whom they may act as agent. Unless otherwise indicated in the applicable prospectus supplement, an agent will be acting on a best efforts basis and a dealer will purchase the common stock as a principal, and may then resell the common stock at varying prices to be determined by the dealer.

We will describe in the applicable prospectus supplement any compensation we pay to underwriters or agents in connection with the offering of our common stock, and any discounts, concessions or commissions allowed by underwriters to participating dealers. Dealers and agents participating in the distribution of the common stock may be deemed to be underwriters, and any discounts and commissions received by them and any profit realized by them on resale of the common stock may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against certain civil liabilities, including liabilities under the Securities Act and to reimburse these persons for certain expenses. We may grant underwriters who participate in the distribution of the common stock we are offering under this prospectus an option to purchase additional shares in connection with the distribution.

To facilitate the offering of our common stock, certain persons participating in the offering may engage in transactions that stabilize, maintain, or otherwise affect the price of the common stock. This may include over-allotments or short sales of the common stock, which involve the sale by persons participating in the offering of more common stock than we sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their option to purchase additional shares, if any. In addition, these persons may stabilize or maintain the price of the common stock by bidding for or purchasing common stock in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering

may be reclaimed if the common stock sold by them is repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the common stock at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

We may indemnify the underwriters, agents or dealers who participate in the distribution of our common stock against certain liabilities, including liabilities under the Securities Act. We may also contribute to payments that the underwriters, dealers or agents or any of their controlling persons may be required to make in respect of such liabilities. Certain underwriters, dealers or agents and their associates may engage in transactions with and perform services for us in the ordinary course of our business.

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LEGAL MATTERS

The validity of the common stock being offered by this prospectus will be passed upon for us by Cooley LLP, San Diego, California.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements (and schedule) included in our Annual Report on Form 10-K for the year ended December 31, 2017, and the effectiveness of our internal control over financial reporting as of December 31, 2017, as set forth in their reports, which are incorporated by reference in this prospectus supplement and elsewhere in the registration statement. Our financial statements (and schedule) are incorporated by reference in reliance on Ernst & Young LLP s reports, given on their authority as experts in accounting and auditing.

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WHERE YOU CAN FIND MORE INFORMATION

We are a reporting company and we file annual, quarterly and current reports, proxy statements and other information with the SEC. We have filed with the SEC a registration statement under the Securities Act with respect to the common stock offered hereby. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement or the exhibits which are part of the registration statement. For further information with respect to us and the common stock offered by this prospectus, we refer you to the registration statement and the exhibits filed as part of the registration statement. Our SEC filings are available to the public from the SEC s website at www.sec.gov. We maintain a website at www.acadia-pharm.com. The information contained in, or that can be accessed through, our website is not part of this prospectus.

The SEC allows us to incorporate by reference the information we file with it, which means that we can disclose important information to you by referring to those documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. We incorporate by reference the following documents we filed with the SEC pursuant to Section 13 of the Exchange Act and any future filings we will make with the SEC under Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act after the date of this prospectus until the termination of the offering of the shares covered by this prospectus (other than information furnished under Item 2.02 or Item 7.01 of Form 8-K):

- Annual Report on Form 10-K for the fiscal year ended December 31, 2017;
- The information specifically incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 31, 2017 from our definitive proxy statement on Schedule 14A (other than information furnished rather than filed) filed with the SEC on April 30, 2018;
- Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2018, June 30, 2018 and September 30, 2018;
- Current Reports on Form 8-K filed on June 8, 2018, July 23, 2018, October 31, 2018, November 5, 2018 and November 20, 2018;
- Description of our common stock contained in our registration statement on Form 8-A dated May 19, 2004; and
- All documents filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus and before the last offering of common stock under this prospectus (excluding any portion of such documents which are furnished and not filed with the SEC).

You may access our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, Proxy Statement, and amendments, if any, to those documents filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act with the SEC free of charge at the SEC s website or our website as soon as reasonably practicable after

such material is electronically filed with, or furnished to, the SEC. The reference to our website does not constitute incorporation by reference of the information contained in our website. We do not consider information contained on, or that can be accessed through, our website to be part of this prospectus or the related registration statement.

You may request a copy of our SEC filings at no cost, by telephoning or writing us at the following address:

Investor Relations

ACADIA Pharmaceuticals Inc.

3611 Valley Centre Drive, Suite 300

San Diego, CA 92130

(858) 558-2871

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PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The following table sets forth the costs and expenses, payable by us in connection with the offering of common stock being registered.

		Amount to Be Paid
Registration fee	$	*
Legal fees and expenses		**
Accounting fees and expenses		**
Transfer agent fees		**
Printing and engraving expenses		**
Miscellaneous		**
Total	$	**

* In accordance with Rule 456(b) and 457(r) we are deferring payment of the registration fee for the securities offered by this prospectus.

** Since an indeterminate amount of securities is covered by this registration statement, the expenses in connection with the issuance and distribution of the securities are not currently determinable.

Item 15. Indemnification of Directors and Officers

Section 102 of the Delaware General Corporation Law allows a corporation to eliminate the personal liability of directors of a corporation to the corporation or its stockholders for monetary damages for a breach of fiduciary duty as a director, except where the director breached his duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of Delaware corporate law or obtained an improper personal benefit.

Section 145 of the Delaware General Corporation Law provides that a corporation has the power to indemnify a director, officer, employee or agent of the corporation and certain other persons serving at the request of the corporation in related capacities against amounts paid and expenses incurred in connection with an action or proceeding to which he is or is threatened to be made a party by reason of such position, if such person shall have acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interest of the corporation, and, in any criminal proceeding, if such person had no reasonable cause to believe his conduct was unlawful; provided that, in the case of actions brought by or in the right of the corporation, no indemnification shall be made with respect to any matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the adjudicating court determines that such indemnification is proper under the circumstances.

Our amended and restated certificate of incorporation and bylaws include provisions that indemnify our directors and officers for actions taken in such capacity, if the actions were taken in good faith and in a manner reasonably believed

to be in our best interests and, in a criminal proceeding, the director or officer had no reasonable cause to believe that his or her conduct was unlawful. A director or officer who is successful in defending a claim will be indemnified for all expenses incurred in connection with his or her defense. We have entered into indemnification agreements with our officers and directors that require us to indemnify such persons against any and all expenses (including attorneys fees), witness fees, damages, judgments, fines, settlements and other amounts incurred in connection with any action, suit or proceeding, whether actual or threatened, to which any such person may be made a party by reason of the fact that such person is or was or at any time becomes a director, an officer or an employee of ACADIA or any of our affiliated enterprises, provided that such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to our best interest and, with respect to any criminal proceeding, had no reasonable cause to believe his or her conduct was unlawful.

We maintain directors and officers insurance providing indemnification for certain of our directors, officers, affiliates, partners and employees for certain liabilities.

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Item 16. Exhibits

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation, as Amended (incorporated by reference to Exhibit 3.1 to the Registrant s Quarterly Report on Form 10-Q, filed August 6, 2015).
3.2	Amended and Restated Bylaws (incorporated by reference to Exhibit 3.1 to the Registrant s Current Report on Form 8-K, filed September 12, 2013).
4.1	Reference is made to Exhibits 3.1 and 3.2 above.
4.2	Form of common stock certificate of the Registrant (incorporated by reference to Exhibit 4.1 to Registration Statement No. 333-52492).
4.3	Form of Warrant to Purchase Common Stock issued to purchasers in a private placement on December 17, 2012 (incorporated by reference to Exhibit 4.4 to Registration Statement No. 333-185639).
4.4	Registration Rights Agreement, dated January 6, 2016, between the Registrant and the investors listed on Schedule A thereto (incorporated by reference to Exhibit 4.1 to the Registrant s Current Report on Form 8-K, filed January 7, 2016).
5.1	Opinion of Counsel.
23.1	Consent of Independent Registered Public Accounting Firm.
23.2	Consent of Counsel (included in Exhibit 5.1).
24.1	Power of Attorney (included on signature page).

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Item 17. Undertakings

(a) The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Securities and Exchange Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20 percent change in the maximum aggregate offering price set forth in the Calculation of Registration Fee table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (a)(1)(i), (a)(1)(ii), and (a)(1)(iii) of this section do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is a part of the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

(i)

Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference

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into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;

(ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;

(iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and

(iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

(b) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant s annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan s annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(c) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in said Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

(d) The undersigned registrant hereby undertakes:

(1) That for purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act of 1933 shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) That for the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

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SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of San Diego, State of California, on November 26, 2018.

ACADIA PHARMACEUTICALS INC.

By: /s/ Stephen R. Davis
Stephen R. Davis
Chief Executive Officer

KNOW ALL PERSONS BY THESE PRESENTS, that each individual whose signature appears below constitutes and appoints Stephen R. Davis and Austin D. Kim, and each of them, his or her true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Registration Statement, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or either of them, or their or his substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following individuals in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Stephen R. Davis Stephen R. Davis	Chief Executive Officer, Director *(Principal Executive Officer and Principal Financial Officer)*	November 26, 2018
/s/ Eric Miller Eric Miller	Senior Director and Controller *(Principal Accounting Officer)*	November 26, 2018
/s/ Stephen R. Biggar Stephen R. Biggar	Chair of the Board	November 26, 2018
/s/ Julian Baker Julian Baker	Director	November 26, 2018

/s/ Laura Brege	Director	November 26, 2018
Laura Brege		
/s/ James Daly	Director	November 26, 2018
James Daly		
/s/ Edmund Harrigan	Director	November 26, 2018
Edmund Harrigan		
/s/ Daniel B. Soland	Director	November 26, 2018
Daniel B. Soland		