IMPROVING LIVES

ACADIA PHARMACEUTICALS INC.

2018 ANNUAL REPORT

ABOUT US

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 developed and commercialized the first and only medicine approved for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis. We also have ongoing clinical development efforts in additional areas with significant unmet need, including dementia-related psychosis, schizophrenia inadequate response, schizophrenia-negative symptoms, major depressive disorder, and Rett syndrome.

To Our Stockholders

I want to thank you for your continued support of our mission at ACADIA Pharmaceuticals.

At ACADIA we are focused on three strategic pillars to achieve our mission. First is to grow NUPLAZID® (pimavanserin) as the only approved treatment for patients with Parkinson's disease psychosis (PDP). Second is to leverage the full potential of pimavanserin by further examining its utility in several additional central nervous system (CNS) disease states with high unmet needs. And third is to expand our pipeline further through focused business development in CNS disorders with high unmet needs.

In 2018 our team successfully executed on all three of our strategic pillars:

We Grew the Sales of NUPLAZID

In 2018 we achieved net sales for the full year of $233.8 million, which represents a 79% increase over the previous year. In 2018 the U.S. FDA approved a single 34-milligram capsule dose formulation of NUPLAZID. The introduction and adoption of the 34-milligram capsule has gone very well and we believe this will result in a more positive patient experience.

Given our continued growth in new patient starts, our continued expansion of our prescriber base, the introduction of the 34 milligram capsule, and NUPLAZID total bottle growth, we are confident in our ability to deliver upon the long-term commercial opportunity in PDP.

We Leveraged Pimavanserin in New Indications

In 2018 we advanced our ongoing late-stage clinical trials designed to further evaluate the safety and efficacy of pimavanserin in patients with dementia-related psychosis, schizophrenia, and major depressive disorder. Notably, in October 2018 we reported robust positive results from our Phase 2 CLARITY study evaluating pimavanserin as an adjunctive therapy for patients with major depressive disorder (MDD).

We Expanded our Pipeline

In 2018 we entered into a North American license agreement for trofinetide from Neuren Pharmaceuticals. 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. Rett syndrome is a highly debilitating rare neurological disorder that occurs primarily in females following apparently normal development for the first six months of life. We plan to initiate a Phase 3 program evaluating trofinetide as potential treatment for Rett syndrome in the fourth quarter of 2019.

Patients need truly innovative medicines that improve their daily lives. We understand these needs and are committed to developing medicines that make a meaningful difference. Our business development efforts are focused on licensing or acquiring novel therapeutic candidates or products that address significant unmet needs for CNS disorders. We have a talented and best-in class R&D and commercial organization with extensive CNS experience, making us an ideal partner for development and commercialization.

We continue to keep patients and their caregivers at the forefront of our business decisions and look forward to an exciting year ahead.

Thank you for your continuing interest in ACADIA and the patients and caregivers we seek to serve.

Stephen R. Davis
Chief Executive Officer
April 2019

ACADIA PHARMACEUTICALS FORM 10-K

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

Form 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2018

Or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission File Number: 000-50768

ACADIA PHARMACEUTICALS INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**06-1376651**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification Number)**
3611 Valley Centre Drive, Suite 300 San Diego, California	**92130**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's telephone number, including area code:

(858) 558-2871

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

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

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

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

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

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

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

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

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

Large accelerated filer ☒	Accelerated filer ☐
Non-accelerated filer ☐ (Do not check if a smaller reporting company)	Smaller reporting company ☐
	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 13(a) of the Exchange Act. ☐

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

As of June 29, 2018, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the registrant's common stock held by non-affiliates of the registrant was approximately $1.2 billion, based on the closing price of the registrant's common stock on the Nasdaq Global Select Market on June 29, 2018 of $15.27 per share.

As of January 31, 2019, 143,882,381 shares of the registrant's common stock, $0.0001 par value, were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement to be filed with the Securities and Exchange Commission by April 30, 2019 are incorporated by reference into Part III of this report.

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ACADIA PHARMACEUTICALS INC.

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PART I

FORWARD-LOOKING STATEMENTS

This report and the information incorporated herein by reference contain forward-looking statements that involve a number of risks and uncertainties, as well as assumptions that, if they never materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements. Although our forward-looking statements reflect the good faith judgment of our management, these statements can only be based on facts and factors currently known by us. Consequently, forward-looking statements are inherently subject to risks and uncertainties, and actual results and outcomes may differ materially from results and outcomes discussed in the forward-looking statements. In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and you are cautioned not to unduly rely upon these statements.

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

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

Item 1. *Business.*

Company Overview

We are a biopharmaceutical company focused on the development and commercialization of innovative medicines that address unmet medical needs in central nervous system, or CNS, 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 in 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 compared to the previous administration of two 17 mg tablets. In addition, the FDA approved a 10 mg NUPLAZID tablet for patients concomitantly receiving strong cytochrome 3A4 inhibitors, which can inhibit the metabolizing 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 are continuing to study the use of pimavanserin in multiple disease states. For example, we believe dementia-related psychosis is 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 October 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 dementia-related psychosis.

According to the National Institute of Mental Health, major depressive disorder, or 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 weight gain or impact on motor function observed. In February 2019, we conducted an End-of-Phase 2 Meeting with the FDA and we plan to initiate a Phase 3 program for pimavanserin as an adjunctive treatment for MDD in the first half of 2019.

We also believe schizophrenia is a disease with multiple unmet or ill-served 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 certain important symptoms of schizophrenia, such as 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 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 study mid-2019. ADVANCE is a Phase 2 study evaluating pimavanserin for adjunctive treatment in patients with negative symptoms of schizophrenia.

In August 2018, we acquired an exclusive North American license to develop and commercialize trofinetide for Rett syndrome and other indications from Neuren Pharmaceuticals Limited, or Neuren. Rett syndrome is a debilitating neurological disorder that occurs predominantly in females following apparently normal development for the first six months of life. Typically, at 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 originally incorporated in Vermont in 1993 as Receptor Technologies, Inc. We reincorporated in Delaware in 1997 and our headquarters are in San Diego, California. We maintain a website at *www.acadia-pharm.com*, to which we regularly post copies of our press releases as well as additional information about us. Our filings with the Securities and Exchange Commission, or SEC, are available free of charge through our website as soon as reasonably practicable after being electronically filed with or furnished to the SEC. Interested persons can subscribe on our website to email alerts that are sent automatically when we issue press releases, file our reports with the SEC or post certain other information to our website. Information contained in our website does not constitute a part of this report or our other filings with the SEC.

We own or have rights to various trademarks, copyrights and trade names used in our business, including ACADIA® and NUPLAZID®. Our logos and trademarks are the property of ACADIA Pharmaceuticals Inc. All other brand names or trademarks appearing in this report are the property of their respective holders. Use or display by us of other parties' trademarks, trade dress, or products in this report is not intended to, and does not, imply a relationship with, or endorsement or sponsorship of us, by the trademark or trade dress owners.

Our Strategy

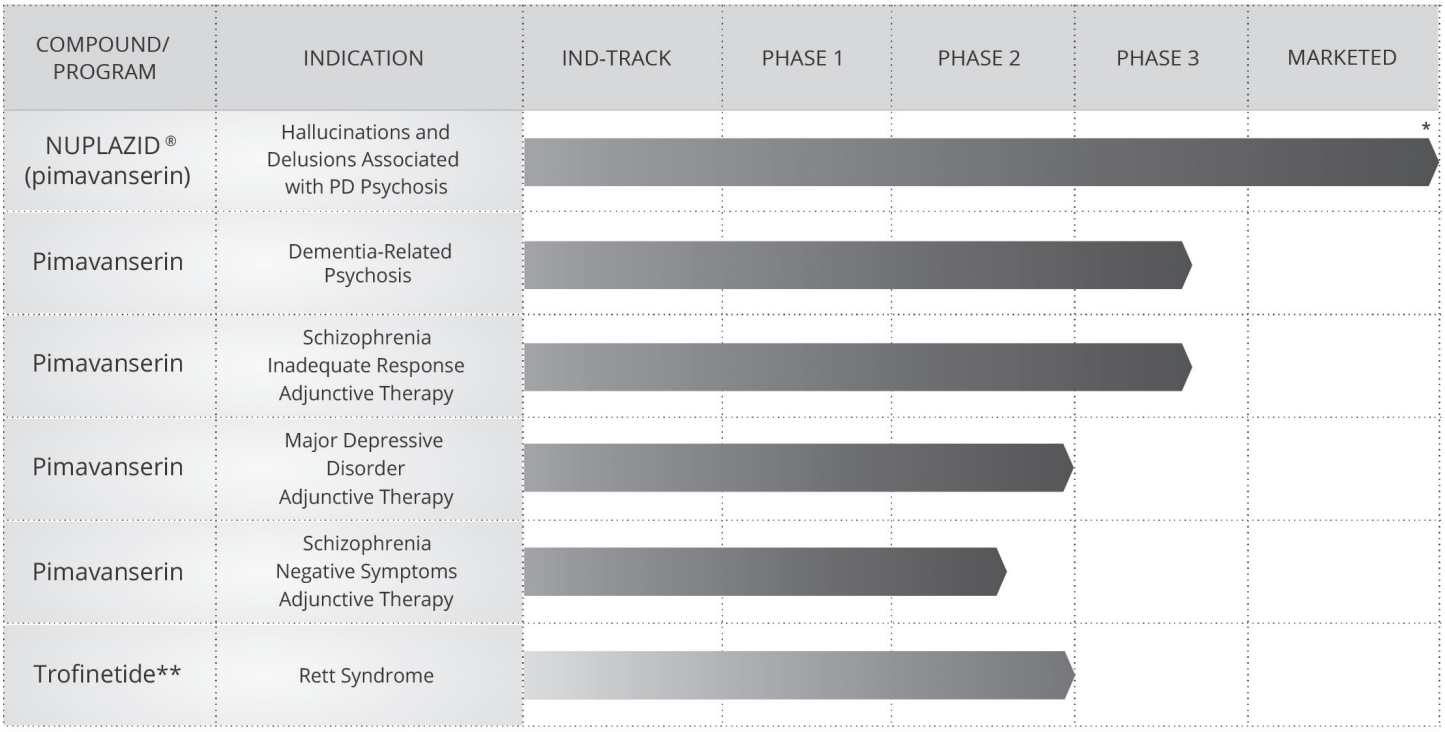
Our strategy is to identify, develop and commercialize innovative drugs that address unmet medical needs in CNS disorders. We have assembled a management team with significant industry experience to lead the discovery, development, and commercialization of our product opportunities. We complement our management team with scientific and clinical advisors, including recognized experts

in the fields of PD Psychosis, Alzheimer's disease, schizophrenia, depression, Rett syndrome and other CNS disorders. Key elements of our strategy are to:

- ***Successfully commercialize NUPLAZID for PD Psychosis in the United States.*** NUPLAZID was approved by the FDA in April 2016 for the treatment of hallucinations and delusions associated with PD Psychosis, and is the only drug approved in the United States for this condition. We launched NUPLAZID in the United States in May 2016 and an important objective is to establish NUPLAZID as the first choice, best choice for PD Psychosis. We employ approximately 150 U.S. sales specialists who are focused on promoting NUPLAZID to physicians who treat PD Psychosis patients, including neurologists, psychiatrists and long-term care physicians.
- ***Leverage the commercial potential of pimavanserin by expanding to additional neurological and psychiatric disorders.*** We intend to continue pursuing the development and commercialization of pimavanserin in additional neurological and psychiatric indications that are underserved by currently available antipsychotics and antidepressants and represent large unmet medical needs. For example, our Phase 3 HARMONY relapse prevention study 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. Also, in October 2018 we announced positive top-line results from CLARITY, a Phase 2 study evaluating pimavanserin as an adjunctive treatment for MDD, and we plan to initiate a Phase 3 program in this patient population in the first half of 2019. We are also testing pimavanserin as an adjunctive therapy in schizophrenia inadequate response and schizophrenia for negative symptoms. In addition to the ongoing development of pimavanserin in these areas, we may also consider additional indications that are a good strategic fit and which have large unmet medical needs.
- ***In-license or acquire complementary products or product candidates.*** Although NUPLAZID (pimavanserin) resulted from internal discoveries, in order to successfully grow our business we plan to in-license or acquire assets, which could include clinical-stage product candidates or commercial-stage products, to leverage our U.S. specialty sales force. For example, in August 2018, we acquired an exclusive North American license to develop and commercialize trofinetide for Rett syndrome and other indications from Neuren Pharmaceuticals.

Our Pipeline

NUPLAZID (pimavanserin) was approved by the FDA in April 2016 for the treatment of hallucinations and delusions associated with PD Psychosis. In addition to PD Psychosis, our pipeline includes multiple product opportunities being explored in clinical development across several CNS disorders with high unmet medical needs. We believe that our product opportunities offer innovative therapeutic approaches and may provide significant advantages relative to current therapies. The following table summarizes our product opportunities and programs:



* NUPLAZID is approved only in the U.S.

** ACADIA has an exclusive license to develop and commercialize trofinetide in North America from Neuren Pharmaceuticals

NUPLAZID (Pimavanserin)

Pimavanserin is a new chemical entity that we discovered and that was approved by the FDA in April 2016 for the treatment of hallucinations and delusions associated with PD Psychosis and is the only drug approved in the United States for this condition and is called NUPLAZID commercially. NUPLAZID is an SSIA preferentially targeting the 5-HT_{2A} receptor, a key serotonin receptor that plays an important role in psychosis. 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 in the treatment of PD Psychosis. We hold worldwide commercialization rights to NUPLAZID for all indications and have established a broad patent portfolio, which includes numerous issued patents in the United States, Europe, and several additional countries. We 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. The recommended dosing of NUPLAZID is 34 mg once a day taken as one 34 mg capsule.

NUPLAZID as a Treatment for PD Psychosis

Parkinson's disease is the second most common neurodegenerative disorder after Alzheimer's disease. According to the Parkinson's Disease Foundation, about one million people in the United States and more than 10 million people globally suffer from this disease. Approximately 50 percent of Parkinson's patients will experience psychosis over the course of their disease. Parkinson's disease is more common in people over 60 years of age and the prevalence of this disease is expected to increase significantly as the population ages.

PD Psychosis is a debilitating disorder commonly characterized by visual hallucinations and delusions that afflicts about 40 percent of the one million Parkinson's disease patients in the United States. The development of psychosis in patients with Parkinson's disease substantially contributes to the burden of Parkinson's disease and deeply affects their quality of life. PD Psychosis is associated with a diminished quality of life, nursing home placement, and increased caregiver stress and burden.

As the first and only drug approved by the FDA for the treatment of hallucinations and delusions associated with PD Psychosis, NUPLAZID provides an innovative and non-dopaminergic approach to the treatment of PD Psychosis without compromising motor control and potentially avoiding many of the debilitating side effects of existing antipsychotics.

In connection with the FDA approval of NUPLAZID, we have committed to conduct post-marketing studies, including a randomized, placebo-controlled withdrawal study in PD Psychosis patients treated with NUPLAZID and randomized, placebo-controlled eight-week studies in predominantly frail and elderly patients that would add to the NUPLAZID safety database by exposing an aggregate of at least 500 patients to NUPLAZID. Through our open-label safety extension study for our Phase 3 studies in PD Psychosis, together with a similar extension study from our earlier Phase 2 PD Psychosis trial, we generated a considerable amount of long-term safety data on NUPLAZID. A total of over 275 patients have been treated with NUPLAZID for at least one year and, of those, at least 170 patients have been treated for at least two years. Our longest single-patient exposure is greater than 11 years. We believe that our experience to date suggests that long-term administration of NUPLAZID is generally safe and well tolerated in this elderly and fragile patient population.

Pimavanserin as a Treatment for Dementia-Related Psychosis

Around 8 million people in the United States are living with dementia and approximately half are diagnosed with the disease. While the primary symptoms of dementia involve cognitive decline, patients with dementia frequently have behavioral symptoms as well. In addition to agitation and aggressive symptoms, they commonly have psychotic symptoms. Studies suggest that approximately 30 percent of patients with dementia have psychosis, commonly consisting of hallucinations and delusions. Patients with dementia-related psychosis share many characteristics and often exhibit similar psychiatric symptoms irrespective of their underlying neurodegenerative disease.

According to the American Psychiatric Association (APA) guidelines "an overwhelming majority" of older adults with dementia will develop psychosis or agitation during the course of their illness. Symptoms are often persistent and occur with increasing frequency as cognition becomes more impaired. Serious consequences have been associated with persistent or severe psychosis in persons with dementia such as repeated hospital admissions, earlier progression to nursing home care, severe dementia, and death. There is currently no approved treatment for dementia-related psychosis. Off-label use of atypical antipsychotics is associated with modest and often equivocal efficacy in these patients. More importantly, use of currently available antipsychotics is associated with a significant acceleration in cognitive decline in patients with dementia as well as numerous off-target toxicities, thus negatively impacting their primary illness. The cognitive effects of treatment with an atypical antipsychotic were evaluated in the National Institute of Mental Health Clinical Antipsychotic Trials of Intervention Effectiveness–Alzheimer's Disease (CATIE-AD) study. In this study, patients on any atypical antipsychotic had significantly greater rates of decline in cognitive function compared to patients on placebo. This pronounced negative impact of currently used antipsychotics on cognitive function is believed to be associated with the common pharmacologic property of these drugs, namely blocking of dopamine receptors. Moreover, anticholinergic activity, which is also present in atypical antipsychotics, is well-known to be associated with cognitive dulling. The lack of selectivity of atypical antipsychotics with respect to receptor activity also results in a number of dose-limiting side effects, such as extrapyramidal symptoms, orthostatic hypotension, hematologic abnormalities, and metabolic, gastrointestinal and sedative effects. These off-target toxicities result in increased risk for falls, infection, aspiration pneumonia, and other serious complications in this vulnerable patient population. With no approved therapies for the treatment of patients with dementia-related psychosis and current off-label use of atypical antipsychotics carrying significant morbidity risks including worsening in cognitive decline and other off target toxicities, we believe that dementia-related psychosis represents an area of high unmet need.

In October 2017, we initiated our HARMONY relapse prevention study, a Phase 3, randomized, double-blind, placebo-controlled study, evaluating the efficacy and safety of pimavanserin for the treatment of hallucinations and delusions associated with dementia-related psychosis. The objective of the study is to evaluate the ability of pimavanserin to prevent relapse of psychotic symptoms in a broad population of patients with the most common subtypes of dementia: 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 dementia-related psychosis.

The HARMONY study includes a 12-week open-label stabilization period during which patients with dementia-related psychosis will be treated with pimavanserin 34 mg once daily. Dose reduction to 20 mg once daily will be allowed if clinically justified. Following the 12-week stabilization period, patients who meet pre-specified criteria for treatment response will then be randomized into the double-blind period of the study to continue their pimavanserin dose (34 mg or 20 mg per day) or be switched to

placebo and followed for up to 26 weeks or until a relapse of psychosis occurs. The primary endpoint in the study is time to relapse in the double-blind period. The study will be conducted globally and is expected to enroll approximately 360 patients.

This Phase 3 development plan is supported by data from two completed clinical studies. In December 2016 we announced positive top-line results from our Phase 2 study, referred to as the -019 Study, examining the safety and efficacy of pimavanserin as a treatment for patients with AD Psychosis, which is a subset of the dementia-related psychosis population. The -019 Study was a double-blind, placebo-controlled exploratory trial designed to evaluate the efficacy and safety of pimavanserin as a treatment for patients with AD Psychosis. A total of 181 patients were enrolled in the study in the United Kingdom. Following a screening period that included brief psycho-social therapy, patients were randomized on a one-to-one basis to receive either 34 mg of pimavanserin or placebo once-daily. The primary endpoint of the study was antipsychotic efficacy as measured by the mean change in the Neuropsychiatric Inventory—Nursing Home, or NPI-NH, Psychosis score (combined hallucinations and delusions domains) from baseline to week six of dosing. The study also assessed additional secondary endpoints, including the cognitive status of patients and the durability of response to pimavanserin, through week 12 of dosing.

Pimavanserin demonstrated efficacy on the primary endpoint of the -019 Study with a 3.76 point improvement in psychosis at week six compared to a 1.93 point improvement for placebo, representing a statistically significant treatment improvement in the NPI-NH Psychosis score (p=0.0451). Baseline mean scores for the pimavanserin and placebo treated groups were 9.52 and 10.00, respectively. Pimavanserin was generally well tolerated and the safety profile was consistent with what has been observed in previous studies. Based on a preliminary analysis of safety data, the most common adverse events reported were falls, urinary tract infection and agitation. The mortality rate was the same in the pimavanserin and placebo treatment groups. Over the course of 12 weeks of treatment, pimavanserin did not impair cognition as measured by the Mini-Mental State Examination, or MMSE, score and was similar to placebo. On the secondary endpoint of mean change in NPI-NH Psychosis score at week 12, pimavanserin maintained the improvement in psychosis observed at the week six primary endpoint, but did not statistically separate from placebo. The mean age of patients in the study was 86 years. Because it has been shown that common symptoms of psychosis in different dementia subtypes need not be etiologically related to respond to pharmacologic treatment, we believe that the results of the -019 Study in patients with AD Psychosis and observations of demented patients in our -020 Study in patients with PD Psychosis, as described below, indicate that pimavanserin may be an effective treatment for the other subgroups of dementia-related psychosis. Results from this Phase 2 study in AD psychosis were presented at the 10th Clinical Trials on Alzheimer's Disease (CTAD) Meeting on November 3, 2017 in Boston.

Additional clinical evidence for efficacy of pimavanserin in dementia-related psychosis was observed in our Phase 3 -020 Study in patients with Parkinson's disease psychosis. Approximately a quarter of the patients enrolled in the -020 Study also suffered from mild dementia. In this pre-specified subgroup, for the primary efficacy analysis those treated with pimavanserin observed a significant improvement in psychosis compared to placebo with a treatment difference of 5.71 points (*p=0.0018*). This effect was larger than the overall average effect observed in the study.

Pimavanserin as an Adjunctive Treatment for Major Depressive Disorder

Major depressive disorder is a condition characterized by depressive symptoms, such as a depressed mood or a loss of interest or pleasure in daily activities for more than two weeks, as well as impaired social, occupational or other important functioning. Studies have shown that the majority of people who suffer from MDD do not respond to initial antidepressant therapy. Also, due to side effects of current therapies, many patients discontinue their medication, significantly increasing their chance of relapse. According to the NIMH, MDD affects approximately 16 million adults in the United States and is the leading cause of disability for ages 15-44.

Preclinical and clinical evidence suggests that the blockade of 5-HT_{2A} receptors improves the clinical effects of selective serotonin reuptake inhibitors, or SSRIs. As an SSIA preferentially targeting 5-HT_{2A} receptors, we believe use of pimavanserin as an adjunctive treatment for MDD may improve outcomes for patients with MDD.

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 weight gain or impact on motor function observed. In February 2019, we conducted an End-of-Phase 2 Meeting with the FDA and we plan to initiate a Phase 3 program for pimavanserin as an adjunctive treatment for MDD in the first half of 2019.

Pimavanserin as an Adjunctive Treatment for Schizophrenia

Schizophrenia is a severe chronic mental illness that involves disturbances in cognition, perception, emotion, and other aspects of behavior. These disturbances may include positive symptoms, such as hallucinations and delusions, and a range of negative symptoms, including loss of interest and emotional withdrawal. Schizophrenia is associated with persistent impairment of a patient's social functioning and productivity. Cognitive disturbances often prevent patients with schizophrenia from readjusting to society. As a result, patients with schizophrenia are normally required to be under medical care for their entire lives. According to the National Institute of Mental Health, or NIMH, approximately one percent of the U.S. population suffers from schizophrenia.

Most patients with schizophrenia in the United States today are treated with second-generation, or atypical, antipsychotics, which induce fewer motor disturbances than typical, or first-generation, antipsychotics, but still fail to address most of the negative symptoms of schizophrenia. In addition, currently prescribed treatments do not effectively address or may exacerbate cognitive disturbances associated with schizophrenia. It is believed that the efficacy of atypical antipsychotics is due to their interactions with dopamine and 5-HT_{2A} receptors. Despite their commercial success, current antipsychotic drugs have substantial limitations, including inadequate efficacy and severe side effects. The side effects induced by the atypical agents may include weight gain, non-insulin dependent (type 2) diabetes, cardiovascular side effects, sleep disturbances, and motor disturbances. We believe that these side effects generally arise either from non-essential receptor interactions or from excessive dopamine blockade.

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

As an SSIA, pimavanserin is a new class of antipsychotic medication with a distinct mechanism of action targeting serotonergic 5-HT_{2A} receptors while avoiding activity at dopamine and other receptors commonly targeted by other antipsychotics which, we believe, may enable pimavanserin to be used in certain treatment approaches to improve the therapy for patients with schizophrenia. We initiated the following studies during the fourth quarter of 2016 to evaluate pimavanserin for adjunctive treatment of schizophrenia in patients with an inadequate response to current antipsychotic therapy and for adjunctive treatment in patients with negative symptoms of schizophrenia:

ENHANCE

In November 2016, we announced that we initiated ENHANCE, a Phase 3 study to evaluate pimavanserin for adjunctive treatment of schizophrenia in patients with an inadequate response to current antipsychotic therapy. According to the American Psychiatric Association, about 30 percent of patients with schizophrenia have inadequate response to antipsychotic medications, meaning that they exhibit improvement, but continue to have residual hallucinations or delusions. As a result, about 25 to 50 percent of schizophrenia patients are treated with two or more antipsychotics. This polypharmacy has led to increased dose-related side effects and complicated dosing regimens that can further contribute to poor treatment compliance and subsequent relapse in these patients. We believe pimavanserin, through its highly selective mechanism of action, could provide an important new option for adjunctive treatment of schizophrenia and improve clinical outcomes by both augmenting the efficacy of currently used antipsychotics and lessening the undesirable side effects associated with polypharmacy.

ENHANCE is a Phase 3, six-week, randomized, double-blind, placebo-controlled, multi-center, outpatient study designed to examine the efficacy and safety of adjunctive use of pimavanserin in patients with schizophrenia who have not achieved an adequate response to their current antipsychotic treatment. Approximately 380 patients will be randomized to receive pimavanserin or placebo, orally, once daily, in addition to their ongoing antipsychotic in a flexible dosing regimen. The starting daily dose of 20 mg of pimavanserin at baseline may be adjusted to 34 mg or 10 mg during the first three weeks of treatment. The primary endpoint of the study is the change from baseline to week six on the Positive and Negative Syndrome Scale, or PANSS, total score. Following participation in ENHANCE, patients will be eligible to enroll in a 52-week open-label extension study. We expect to report top-line results of the ENHANCE study mid-2019.

ADVANCE

In November 2016, we announced that we initiated ADVANCE, a Phase 2 study to evaluate pimavanserin for adjunctive treatment in patients with negative symptoms of schizophrenia. Studies show that about 40 to 50 percent of schizophrenia patients suffer from prominent negative symptoms. While currently available antipsychotic treatments for schizophrenia target positive symptoms, most patients remain functionally impaired because of negative symptoms, cognitive deficits and limited social function. There is currently no drug approved by the FDA for the treatment of the negative symptoms of schizophrenia.

ADVANCE is a Phase 2, 26-week, randomized, double-blind, placebo-controlled, multi-center study designed to examine the efficacy and safety of adjunctive use of pimavanserin in patients with schizophrenia who have predominant negative symptoms. Approximately 380 patients will be randomized to receive either pimavanserin or placebo, orally, once daily, in addition to their ongoing antipsychotic in a flexible dosing regimen. The starting daily dose of 20 mg of pimavanserin at baseline may be adjusted to 34 mg or 10 mg during the first eight weeks of treatment. The primary endpoint of the study is the change from baseline to week 26 on the Negative Symptom Assessment-16, or NSA-16, total score. Following participation in ADVANCE, patients will be eligible to enroll in a 52-week open-label extension study.

Trofinetide

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. In the central nervous system, IGF-1 is produced by both of the major types of brain cells – neurons and glia. IGF-1 in the brain is critical for both normal development and for response to injury and disease. Trofinetide has been granted FDA Fast Track Status and Orphan Drug Designation in the U.S. and Orphan Designation in Europe.

Trofinetide as a Treatment for Rett Syndrome

Rett syndrome is a debilitating neurological disorder that occurs primarily in females following apparently normal development for the first six months of life. Rett syndrome has been most often misdiagnosed as autism, cerebral palsy, or non-specific developmental delay. Rett syndrome is caused by mutations on the X chromosome on a gene called MeCP2. There are more than 200 different mutations found on the MeCP2 gene that interfere with its ability to generate a normal gene product. Rett syndrome occurs worldwide in approximately one of every 10,000 to 15,000 female births causing problems in brain function that are responsible for cognitive, sensory, emotional, motor and autonomic function. 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, an abnormal side-to-side curvature of the spine (scoliosis) and sleep disturbances. Currently, there are no approved medicines approved 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.

Competition

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

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 generic drugs quetiapine, clozapine, olanzapine, risperidone and aripiprazole.

If approved, pimavanserin for the treatment of dementia-related psychosis would compete with off-label use of antipsychotic drugs, including 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 plc.

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 MDD, if approved for that indication, would compete with Rexulti and generic adjunctive atypical antipsychotics, including aripiprazole, quetiapine and risperidone.

There are currently no approved medications for the treatment of Rett syndrome. Trofinetide, if approved would compete with off label usage of generic prescription medications targeted at individual symptoms of Rett syndrome, including antipsychotics, antidepressants and benzodiazepines. There are multiple academic institutions and six other pharmaceutical companies conducting clinical trials for the treatment of various symptoms of Rett syndrome. Additionally AveXis/Novartis has a gene therapy program in Rett syndrome with a current projected FDA filing date of 2022.

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

- identifying and validating targets;
- screening compounds against targets;
- preclinical 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 advantages in the following areas:

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

Smaller companies also may prove to be significant competitors, particularly through proprietary research discoveries and collaborative arrangements with large pharmaceutical and established biotechnology companies. Many of our competitors have products that have been approved or are in advanced development and may develop superior technologies or methods to identify and validate drug targets and to discover novel small molecule drugs. We face competition from other companies, academic institutions, governmental agencies and other public and private research organizations for collaborative arrangements with pharmaceutical and biotechnology companies, in recruiting and retaining highly qualified scientific, sales and marketing, and management personnel and for licenses to additional technologies. Our competitors, either alone or with their collaborators, may succeed in developing technologies or drugs that are more effective, safer, and more affordable, or more easily administered than ours and may achieve patent protection or commercialize drugs sooner than us. 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.

Intellectual Property

We currently hold 32 issued U.S. patents and a significant number of related issued foreign patents. All of these patents originated from inventions made by us. Patents and other proprietary intellectual property rights are an essential element of our business. Our strategy is to file patent applications in the United States and any other country that represents an important potential commercial market to us. In addition, we seek to protect our technology and inventions (and improvements to inventions) that are important to the development of our business. Our patent applications claim proprietary technology, including chemical synthetic or manufacturing methods, drug assays, novel compounds, compositions, formulations and methods of treatment. We also rely upon trade secrets, including technologies that may be used to discover and validate targets, to identify and develop novel drugs, as well as manufacturing or clinical development technologies, among others. We protect our trade secrets by, among other things, requiring employees and third parties who have access to our proprietary information to sign confidentiality and nondisclosure agreements. We are a party to various license agreements that give us rights to use certain technologies in our research and development.

Pimavanserin

To date, twenty-seven U.S. patents have been issued to us that relate to pimavanserin, NUPLAZID and methods of use. Twelve of these are Orange Book-listed patents that relate to pimavanserin, NUPLAZID and our approved indication, and cover the general formula of the compound, the composition of matter, with claims specifically directed to pimavanserin and salts thereof, the specific polymorph form of pimavanserin, and the use thereof for treating our approved indication. The composition of matter U.S. patent covering pimavanserin and salts thereof is currently set to expire in 2027. The patents covering the polymorph form and the use of pimavanserin or NUPLAZID for our approved indication are currently set to expire between 2022 and 2028. These patent terms include adjustments made by the U.S. Patent and Trademark Office (the "PTO"), but not patent term extensions.

We have filed patent term extension applications on three U.S. patents. The PTO has not completed its review of these applications. In the United States, we are permitted to extend the term of one U.S. patent for pimavanserin or the use thereof. Accordingly, on completion of the PTO's review of our patent term extension applications, we must select one of the three patents to which any patent term extension granted will attach. Patent terms may be subject to change not only due to potential patent term extensions but also to any terminal disclaimer that reduces patent term, as well as other factors. Because the U.S. patent laws and judicial interpretations thereof change, modifications or new interpretations of the laws may impact our patent terms.

The remaining 15 U.S. patents relating to pimavanserin that have been issued to us cover methods of use of pimavanserin for treating AD Psychosis, Alzheimer's disease indications, schizophrenia, bipolar disorder, Lewy body dementia, sleep disorders, hallucinations, delusions, other methods of treatment and methods of producing pimavanserin. We have a significant number of related issued foreign patents that specifically cover pimavanserin and polymorphs thereof in Europe and Asia as well as in Australia, Canada, Mexico and other countries. We continue to file and prosecute patent applications directed to pimavanserin, formulations of pimavanserin and to methods of treating various diseases using pimavanserin, either alone or in combination with other agents, worldwide.

We entered into a license agreement in 2006 for certain intellectual property rights from the Ipsen Group that complement the intellectual property portfolio for our serotonin platform, including pimavanserin. We are required to pay to the Ipsen Group royalties of up to two percent of net product sales of NUPLAZID pursuant to the agreement.

Collaboration Agreements

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

Government Regulation

Our business activities, including the manufacturing and marketing of NUPLAZID and our potential products and our ongoing research and development activities, are subject to extensive regulation by numerous governmental authorities in the United States and other countries. Before marketing in the United States, any new drug developed by us must undergo rigorous preclinical testing, clinical trials and an extensive regulatory clearance process implemented by the FDA under the Federal Food, Drug, and Cosmetic Act, as amended. The FDA regulates, among other things, the development, testing, manufacture, safety, efficacy, record keeping, labeling, storage, approval, advertising, promotion, import, export, sale and distribution of biopharmaceutical products. The regulatory review and approval process, which includes preclinical testing and clinical trials of each product candidate, is lengthy, expensive and uncertain. Moreover, government coverage and reimbursement policies will both directly and indirectly impact our ability to successfully commercialize NUPLAZID and any future approved products, and such coverage and reimbursement policies will be impacted by enacted and any applicable future healthcare reform and drug pricing measures. In addition, we are subject to state and federal laws, including, among others, anti-kickback laws, false claims laws, data privacy and security laws, and transparency laws that restrict certain business practices in the pharmaceutical industry.

In the United States, drug product candidates intended for human use undergo laboratory and animal testing until adequate proof of safety is established. Clinical trials for new product candidates are then typically conducted in humans in three sequential phases that may overlap. Phase 1 trials involve the initial introduction of the product candidate into healthy human volunteers. The emphasis of Phase 1 trials is on testing for safety or adverse effects, dosage, tolerance, metabolism, distribution, excretion and clinical pharmacology. Phase 2 involves studies in a limited patient population to determine the initial efficacy of the compound for specific targeted indications, to determine dosage tolerance and optimal dosage, and to identify possible adverse side effects and safety risks. Once a compound shows initial evidence of effectiveness and is found to have an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to more fully evaluate clinical outcomes. Before commencing clinical investigations in humans, we or our collaborators must submit an Investigational New Drug Application, or IND, to the FDA.

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

To establish a new product candidate's safety and efficacy, the FDA requires companies seeking approval to market a drug product to submit extensive preclinical and clinical data, along with other information, for each indication for which the product will be labeled. The data and information are submitted to the FDA in the form of a New Drug Application, or NDA, which must be accompanied by payment of a significant user fee unless a waiver or exemption applies. Generating the required data and information for an NDA takes many years and requires the expenditure of substantial resources. Information generated in this process is susceptible to varying interpretations that could delay, limit or prevent regulatory approval at any stage of the process. The failure to demonstrate adequately the quality, safety and efficacy of a product candidate under development would delay or prevent regulatory approval of the product candidate. Under applicable laws and FDA regulations, each NDA submitted for FDA approval is given an internal administrative review within 60 days following submission of the NDA. If deemed sufficiently complete to permit a substantive review, the FDA will "file" the NDA. The FDA can refuse to file any NDA that it deems incomplete or not properly reviewable. The FDA has established internal goals of eight months from submission for priority review of NDAs that cover product candidates that offer major advances in treatment or provide a treatment where no adequate therapy exists, and 12 months from submission for the standard review of NDAs. However, the FDA is not legally required to complete its review within these periods, these performance goals may change over time and the review is often extended by FDA requests for additional information or clarification. Moreover, the outcome of the review, even if generally favorable, may not be an actual approval but a "complete response letter" that describes additional work that must be done before the NDA can be approved. Before approving an NDA, the FDA can choose to inspect the facilities at which the product is manufactured and will not approve the product unless the manufacturing facility complies with GMPs. The FDA may also audit sites at which clinical trials have been conducted to determine compliance with GCPs and data integrity. The FDA's review of an NDA may also involve review and recommendations by an independent FDA advisory committee, particularly for novel indications. The FDA is not bound by the recommendation of an advisory committee.

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

Before receiving FDA approval to market a potential product, we or our collaborators must demonstrate through adequate and well-controlled clinical studies that the potential product is safe and effective in the patient population that will be treated. In addition, under the Pediatric Research Equity Act, or PREA, an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective, unless a waiver applies. If regulatory approval of a potential product is granted, this approval will be limited to those disease states and conditions for which the product is approved. Marketing or promoting a drug for an unapproved indication is generally prohibited. Furthermore, FDA approval may entail ongoing requirements for risk management, including post-marketing, or Phase 4, studies. Even if approval is obtained, each marketed product, is subject to payment of a significant annual program user fee and continuing review and periodic inspections by the FDA. Discovery of previously unknown problems with a product, manufacturer or facility may result in restrictions on the product or manufacturer, including labeling changes, warning letters, costly recalls or withdrawal of the product from the market.

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

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

We and our collaborators and contract manufacturers also are required to comply with the applicable FDA GMP regulations. GMP regulations include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation. Manufacturing facilities are subject to inspection by the FDA. These facilities must be approved before we can use them in commercial manufacturing of our potential products and must maintain ongoing compliance for commercial

product manufacture. The FDA may conclude that we or our collaborators or contract manufacturers are not in compliance with applicable GMP requirements and other FDA regulatory requirements, which may result in delay or failure to approve applications, warning letters, product recalls and/or imposition of fines or penalties.

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

In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of pharmaceutical products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain.

Outside of the United States, our ability to market a product is contingent upon receiving a marketing authorization from the appropriate regulatory authorities. The requirements governing the conduct of clinical trials, marketing authorization, pricing and reimbursement vary widely from country to country. At present, foreign marketing authorizations are applied for at a national level, although within the European Community, or EC, centralized registration procedures are available to companies wishing to market a product in more than one EC member state. If the regulatory authority is satisfied that adequate evidence of safety, quality and efficacy has been presented, marketing authorization will be granted. This foreign regulatory approval process involves all of the risks associated with FDA marketing approval discussed above. In addition, foreign regulations may include applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or other transfers of value to healthcare professionals and entities.

Coverage and Reimbursement

Sales of NUPLAZID and of our product candidates, if approved, depend and will depend, in part, on the extent to which such products will be covered by third-party payors, such as government health care programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly limiting coverage and/or reducing reimbursements for medical products and services. A third-party payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage for the drug product. In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party payor reimbursement or a decision by a third-party payor to not cover NUPLAZID or any future approved products could reduce physician usage of our products, and have a material adverse effect on our sales, results of operations and financial condition.

In the United States, the Medicare Part D program provides a voluntary outpatient drug benefit to Medicare beneficiaries for certain products. NUPLAZID is available for coverage under Medicare Part D, but the individual Part D plans offer coverage subject to various factors such as those described above. In addition, while Medicare Part D plans have historically included "all or substantially all" drugs in the following designated classes of "clinical concern" on their formularies: anticonvulsants, antidepressants, antineoplastics, antipsychotics, antiretrovirals, and immunosuppressants, the Centers for Medicare and Medicaid Services, or CMS, has in the past proposed, but not adopted, changes to this policy. If this policy is changed in the future and if CMS no longer considers the antipsychotic class to be of "clinical concern", Medicare Part D plans would have significantly more discretion to reduce the number of products covered in that class, including coverage of NUPLAZID. Furthermore, private third-party payors often follow Medicare coverage policies and payment limitations in setting their own coverage policies.

Healthcare Laws and Regulations

We are subject to healthcare regulation and enforcement by the federal government and the states and foreign governments in which we conduct our business. The healthcare laws and regulations that may affect our ability to operate include the following:

- The federal Anti-Kickback Statute makes it illegal for any person or entity to knowingly and willfully, directly or indirectly, solicit, receive, offer, or pay any remuneration that is in exchange for or to induce the referral of business,

including the purchase, order, lease of any good, facility, item or service for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. The term "remuneration" has been broadly interpreted to include anything of value.

- Federal false claims and false statement laws, including the federal civil False Claims Act, prohibits, among other things, any person or entity from knowingly presenting, or causing to be presented, for payment to, or approval by, federal programs, including Medicare and Medicaid, claims for items or services, including drugs, that are false or fraudulent.
- The U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors or making any false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services.
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their implementing regulations, imposes obligations on certain types of individuals and entities regarding the electronic exchange of information in common healthcare transactions, as well as standards relating to the privacy and security of individually identifiable health information. In addition, the European Union, or EU, has established its own data security and privacy legal framework, including but not limited to the recently adopted European General Data Protection Regulation (EU) 2016/79, or GDPR, which contains new provisions specifically directed at the processing of health information, higher sanctions than previous EU data protection laws and extra-territoriality measures intended to bring non-EU companies under the regulation. We currently conduct clinical trials in the EU and will need to be compliant with these requirements. We anticipate that over time we may expand our business operations to include additional operations in the EU. With such expansion, we would be subject to increased governmental regulation in the EU countries in which we might operate, including the GDPR.
- The federal Physician Payments Sunshine Act 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, with specific exceptions, to report annually to CMS information related to payments or 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.

Also, many states have similar laws and regulations, such as anti-kickback and false claims laws that may be broader in scope and may apply regardless of payor, in addition to items and services reimbursed under Medicaid and other state programs. Additionally, we may be subject to state laws that require pharmaceutical companies to comply with the federal government's and/or pharmaceutical industry's voluntary compliance guidelines, state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures, state laws that require drug manufacturers to report information on the pricing of certain drugs, state and local laws that require the registration of pharmaceutical sales representatives, as well as state and foreign laws governing the privacy and security of health information, many of which differ from each other in significant ways and often are not preempted by HIPAA.

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 significant 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.

Additionally, to the extent that our product is sold in a foreign country, we may be subject to similar foreign laws.

Healthcare Reform

The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. By way of example, in March 2010, the ACA was signed into law, which intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add transparency requirements for the healthcare and health insurance industries, impose taxes and fees on the health industry and impose additional health policy reforms.

Among the provisions of the ACA of importance to NUPLAZID and our product candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1 percent and 13.0 percent of the average manufacturer price for branded and generic drugs, respectively;

- extension of a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133 percent of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- a Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70 percent point-of-sale discounts to negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for a manufacturer's outpatient drugs to be covered under Medicare Part D;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- a requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

There have been judicial and Congressional 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, or 2017 Tax Act, 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". 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. 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. In July 2018, CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 2018, a federal judge in Texas ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the 2017 Tax Act. While the judge, as well as the Trump administration and CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the ACA will impact the ACA.

Other legislative changes have been proposed and adopted in the United States since the ACA. Through the process created by the Budget Control Act of 2011, there are automatic reductions of Medicare payments to providers up to 2 percent per fiscal year, which went into effect in April 2013 and, following passage of the BBA, will remain in effect through 2027 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to certain providers.

Moreover, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their commercial products. 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. 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. Additionally, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase 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 U.S. 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. For example, in September 2018, CMS announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019, in October 2018, CMS proposed a new rule that would require direct-to-consumer television advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product, and on January 31, 2019, the HHS Office of Inspector General proposed modifications to

federal Anti-Kickback Statute safe harbors which, among other things, may affect rebates paid by manufacturers to Medicare Part D plans, the purpose of which is to further reduce the cost of drug products to consumers. Although a number of these, and other 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. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological 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.

We expect that healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and lower reimbursement, and additional downward pressure on the price that we receive for NUPLAZID and any future approved products. We cannot predict what healthcare reform initiatives may be adopted in the future. Additionally, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

Manufacturing and Distribution

We currently outsource, and plan to continue to outsource, manufacturing activities for NUPLAZID, as well as for our existing and future product candidates for development and commercial purposes. We believe this manufacturing strategy will enable us to direct our financial resources to our commercial activities and to the ongoing development of pimavanserin without devoting the substantial resources and capital required to build manufacturing facilities.

During 2015, we licensed worldwide intellectual property rights related to pimavanserin in certain indications to ACADIA Pharmaceuticals GmbH, our wholly-owned Swiss subsidiary. Our active pharmaceutical ingredient, or API, has been manufactured in Switzerland for over 10 years and we anticipate continuing to manufacture in Switzerland. ACADIA Pharmaceuticals GmbH manages the worldwide supply chain of pimavanserin API.

ACADIA Pharmaceuticals GmbH has contracted with Siegfried AG, or Siegfried, to manufacture the API to be used in the manufacture of NUPLAZID for commercial use. Under the manufacturing agreement, ACADIA Pharmaceuticals GmbH has agreed to purchase from Siegfried specified percentages of our commercial requirements of API for the United States and Europe. The parties may also agree in the future on additional services under the manufacturing agreement with respect to non-commercial supply or development activities. The term of the manufacturing agreement ends in December 2021 and will automatically renew for subsequent two-year terms unless either party provides timely notice of its intent not to renew, or unless the manufacturing agreement is terminated earlier pursuant to its terms. Either party may terminate the manufacturing agreement prior to expiration upon an uncured material breach by the other party, upon the dissolution or liquidation of the other party, the commencement of insolvency procedures that are not dismissed within a certain period of time, the appointment of any receiver, trustee or assignee to take possession of the properties of the other party or the cessation of all or substantially all of the other party's business operations, upon certain continuing patent infringement, regulatory litigation or other legal proceedings involving the manufacture of API, upon a continuing force majeure affecting the other party, or if no services are currently being provided under the manufacturing agreement. Additionally, if the parties agree on development services under the manufacturing agreement, the parties may terminate such services by mutual agreement if reasonable efforts to achieve the goals of such services fail. ACADIA Pharmaceuticals GmbH also may terminate any services under the manufacturing agreement for any reason on 90 days' prior notice to Siegfried, subject to the requirements of the manufacturing agreement.

We have contracted with Patheon Pharmaceuticals Inc., or Patheon, to manufacture NUPLAZID drug product for commercial use in the United States. Under the manufacturing agreement, we have agreed to purchase from Patheon a specified percentage of our commercial requirements of NUPLAZID for the United States. The term of the manufacturing agreement ends in December 2020 and will automatically renew for subsequent two-year terms unless either party provides timely notice of its intent not to renew, or unless the manufacturing agreement is terminated early pursuant to its terms. Each party may terminate the manufacturing agreement prior to expiration upon the uncured material breach by the other party, upon the bankruptcy or insolvency of the other party or in the event of a continuing force majeure event affecting the other party. The manufacturing agreement will also terminate if we provide notice to Patheon that we no longer require manufacturing services because NUPLAZID has been discontinued. Additionally, we may terminate the manufacturing agreement, subject to certain limitations, if any regulatory authority takes any action or raises any objection that prevents us from continuing to commercialize NUPLAZID or takes an enforcement action against Patheon’s manufacturing site that relates to NUPLAZID or could reasonably be expected to adversely affect Patheon’s ability to supply

NUPLAZID, if we determine to discontinue commercialization of NUPLAZID for safety or efficacy reasons, or if Patheon uses any debarred person in performing its service obligations under the manufacturing agreement. We also may terminate the manufacturing agreement for any other reason on three years' prior notice to Patheon. Additionally, Patheon may terminate the manufacturing agreement if we assign the manufacturing agreement or any of our rights under the manufacturing agreement to a Patheon competitor.

We have also contracted with Catalent Pharma Solutions, LLC, or Catalent, to manufacture NUPLAZID drug product capsules for commercial use in the United States. Under the supply agreement, Catalent has agreed to manufacture and supply NUPLAZID 34 mg capsule drug product, referred to as NUPLAZID capsules, for our commercial use in the United States, Canada and Europe, and we have agreed to purchase from Catalent a specified percentage of our commercial requirements of NUPLAZID capsules for such territory, subject to a minimum annual purchase commitment of NUPLAZID capsules. Catalent will manufacture NUPLAZID capsules using API supplied by another third-party manufacturer. Under the supply agreement, Catalent will also perform specified validation services. The term of the supply agreement extends for five years from the date that Catalent is first approved by a regulatory authority in the United States, Canada or Europe to produce NUPLAZID capsules, and will automatically renew for subsequent two-year terms unless either party provides timely notice of its intent not to renew, or unless the supply agreement is terminated early pursuant to its terms. Either we or Catalent may terminate the supply agreement prior to expiration upon the bankruptcy or insolvency of the other party or upon an uncured material breach by the other party. We may terminate the supply agreement, subject to certain limitations, if any regulatory authority takes any enforcement or other action against Catalent's facility which affects Catalent's ability to manufacture NUPLAZID capsules, or takes any action or raises any objection that prevents us from manufacturing, importing, exporting, purchasing or selling NUPLAZID capsules, if we determine to discontinue commercialization of NUPLAZID capsules in the United States for safety or efficacy reasons, or if Catalent uses any debarred person in performing its service obligations under the supply agreement. The FDA approved our NDA for the 34 mg NUPLAZID capsule formulation in June 2018 and was made commercially available in August 2018.

We sell NUPLAZID to a limited number of specialty pharmacies, or SPs, and specialty distributors, or SDs, which we collectively refer to as our customers. SPs subsequently dispense NUPLAZID to patients based on the fulfillment of a prescription and SDs subsequently sell NUPLAZID to government facilities, long-term care pharmacies, and in-patient hospital pharmacies. Four customers, each based in the United States, accounted for approximately 85 percent of our total revenue for the year ended December 31, 2018. We have retained third-party service providers to perform a variety of functions related to the distribution of NUPLAZID, including warehousing, customer service, order-taking, invoicing, collections, and shipment and returns processing.

Sales and Marketing

We have a U.S. sales force of approximately 150 sales specialists who are focused on promoting NUPLAZID to physicians who treat PD Psychosis patients, including neurologists, psychiatrists and long-term care physicians. This sales force is supported by an experienced sales leadership team of regional sales managers and account managers, and our experienced commercial team comprised of experienced professionals in marketing, access and reimbursement, managed markets, marketing research, commercial operations, and sales force planning and management. In addition, our commercial infrastructure includes capabilities in manufacturing, medical affairs, quality control, and compliance.

We launched NUPLAZID in May 2016, and our focus is to continue to establish NUPLAZID as the first choice, best choice for patients with PD Psychosis. In order to help us achieve this goal, we are continuing to increase awareness of NUPLAZID and PD Psychosis with a prescriber and patient education campaign consisting of key opinion leader speaker programs, attendance at medical meetings, multimedia campaigns, and direct-to-patient programs.

In selected markets outside of the United States in which NUPLAZID may be approved, if any, we may choose to commercialize NUPLAZID independently or by establishing one or more strategic alliances.

Long-Lived Assets

Our tangible long-lived assets, comprised of property and equipment totaled $3.3 million, $2.7 million, and $3.1 million as of December 31, 2018, 2017 and 2016, respectively. All of our tangible long-lived assets are located in the United States.

Employees

At December 31, 2018, we had approximately 430 employees. Of this workforce, approximately 135 employees were engaged in research and development activities, 90 were engaged in administrative activities such as finance, legal, and information technology, and 205 were engaged in sales, commercial operations and marketing. None of our employees is represented by a collective bargaining agreement, nor have we experienced work stoppages. We believe that our relations with our employees are good.

Item 1A. ***Risk Factors.***

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

Risks Related to Our Business

Our prospects are highly dependent on the 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.

If we do not obtain regulatory approval of NUPLAZID for other indications in the United States, or for any indication in foreign jurisdictions, or regulatory approval of trofinetide for Rett syndrome, we will not be able to market NUPLAZID for other indications or in other jurisdictions or market trofinetide at all, 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, 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. We plan to initiate a Phase 3 program for pimavanserin as an adjunctive treatment for major depressive disorder in the first half of 2019 and we plan to initiate a Phase 3 study of trofinetide for Rett syndrome in the second half of 2019. 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 or trofinetide 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 or to submit trofinetide for approval for Rett syndrome. 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 or any marketing approval for trofinetide, we will never be able to commercialize NUPLAZID for any other indication in the United States or for any indication in any other jurisdiction or be able to commercialize trofinetide at all. 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.

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 and we have submitted a supplemental NDA, or sNDA, for the completed CYP3A4 study, 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.

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 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.

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 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. 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 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.

For example, 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, or 2017 Tax Act, 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". 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. 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 for 2019 the percentage that a drug manufacturer must discount the cost of prescription drugs from 50 percent 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. In July 2018, CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 2018, a federal judge in Texas ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the 2017 Tax Act. While the judge, as well as the Trump administration and CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the ACA will impact the ACA and our business.

Other legislative changes have been proposed and adopted in the United States since the ACA. Through the process created by the Budget Control Act of 2011, there are automatic reductions of Medicare payments to providers up to 2 percent per fiscal year, which went into effect in April 2013 and, following passage of the BBA, will remain in effect through 2027 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to certain providers.

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. Additionally, the Trump administration released a "Blueprint", or plan, to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug 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. For example, in September 2018, CMS announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019, in October 2018, CMS proposed a new rule that would require direct-to-consumer television advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product, and on January 31, 2019, the HHS Office of Inspector General proposed modifications to federal Anti-Kickback Statute safe harbors which, among other things, may affect rebates paid by manufacturers to Medicare Part D plans, the purpose of which is to further reduce the cost of drug products to consumers. Although a number of these, and other 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 increasingly passed legislation and implemented 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 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 their 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 certain healthcare providers as well as their business associates, individuals or entities that perform certain services involving the use or disclosure of individually identifiable health information on behalf of a covered entity;
- 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 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 (EU) 2016/679, 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.

Additionally, California recently enacted legislation that has been dubbed the first "GDPR-like" law in the United States. Known as the California Consumer Privacy Act, or CCPA, it creates new individual privacy rights for consumers (as that word is broadly defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. When it goes into effect on January 1, 2020, the CCPA will require covered companies to provide new disclosures to California consumers, provide such consumers new ways to opt-out of certain sales of personal information, and allow for a new cause of action for data breaches. Legislators have stated that amendments will be proposed to the CCPA before it goes into effect, but it remains unclear what, if any, modifications will be made to this legislation or how it will be interpreted. As currently written, the CCPA will likely impact (possibly significantly) our business activities and exemplifies the vulnerability of our business to not only cyber threats but also the evolving regulatory environment related to personal data and protected health information.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. 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 HHS Office of Inspector General 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 a timely basis could result in significant civil monetary penalties 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 civil 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 HHS Office of Inspector General, 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 civil 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 December 31, 2018, we had an accumulated deficit of approximately $1.5 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.

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 $473.5 million at December 31, 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 our planned development activities for Trofinetide
- 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;
- 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.

Changes in funding for the FDA and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including beginning on December 22, 2018 and ending on January 25, 2019, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical government employees and stop critical activities. If repeated or prolonged government shutdowns occur, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, and negatively impact other government operations on which we rely, which could have a material adverse effect on our business.

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 may not be 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, or CLARITY, for which we announced positive top-line results in October 2018, 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 and CLARITY. 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.

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 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. In October 2018, we announced positive top-line results from CLARITY, a Phase 2 study evaluating pimavanserin as an adjunctive treatment for major depressive disorder and we plan to initiate a Phase 3 program in the first half of 2019. 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;
- 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;
- 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 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 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 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 December 31, 2018, we employed approximately 430 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.

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.

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;
- 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.

U.S. federal income tax reform could adversely affect our business and financial condition.

On December 22, 2017, U.S. federal income tax legislation was signed into law (H.R. 1, "An Act to provide for reconciliation pursuant to titles II and V of the concurrent resolution on the budget for fiscal year 2018", informally titled the Tax Cuts and Jobs Act, or the 2017 Tax Act), which significantly revised the Internal Revenue Code of 1986, as amended, or the Code. The 2017 Tax Act, 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 repeal of the alternative minimum tax for corporations, 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 2017 Tax Act 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 2017 Tax Act.

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

As of December 31, 2018, we had federal, state and foreign net operating loss carryforwards of $393.0 million, $339.0 million and $771.9 million, respectively. The majority of our net operating loss carryforwards will begin to expire, if not utilized, beginning in 2023. These net operating loss carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the 2017 Tax Act, 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 2017 Tax Act. 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 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.

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 position, results of operations or reported cash flows. In February 2016, the FASB issued Accounting Standards Update (ASU) No. 2016-02, *Leases (Topic 842)*, which requires a lessee to recognize a lease liability and a right-of-use asset for all leases with lease terms of more than 12 months. We adopted this new standard for the year beginning January 1, 2019 and have elected to apply the new standard using the modified retrospective method using the effective date as the date of initial application. We expect adoption of this standards to have a material effect on our consolidated balance sheets and 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;
- 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 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 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 compromised by disclosure during this type of litigation. In addition, during the course of this kind of litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the trading price of our common stock.

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

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

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

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

Risks Related to Our Industry

We 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.

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.

While there are no approved medications for the treatment of Rett syndrome, trofinetide, if approved for Rett syndrome would compete with off label usage of generic prescription medications targeted at individual symptoms of Rett syndrome. These include antipsychotics including risperidone and aripiprazole; antidepressants sertraline and citalopram; and benzodiazepines clonazepam and diazepam. There are multiple academic institutions and six other pharmaceutical companies conducting clinical research in Rett syndrome. While other pharmaceutical companies are studying compounds for the associated symptoms of Rett syndrome (seizures – Ultragenyx, Anavex, GW Pharmaceuticals; respiratory issues – Newron, Neurolixis), these ongoing clinical trials have identified secondary outcomes assessing impact on overall disorder and some may launch in advance of trofinetide. Rett specific scales are being used in these trials including the RSBQ (Rett syndrome Behavioral Questionaire) which is being used in the trofinetide Phase 3 trial. Additionally AveXis/Novartis has a gene therapy program in Rett syndrome with a current projected FDA filing date of 2022.

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;
- 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.

We are dependent on information technology systems, infrastructure and data, which exposes us to data security risks.

We are dependent upon our own or third-party information technology systems, infrastructure and data, including mobile technologies, to operate our business. The multitude and complexity of our computer systems may make them vulnerable to service interruption or destruction, disruption of data integrity, malicious intrusion, or random attacks. Likewise, data privacy or security incidents or breaches by employees or others may pose a risk that sensitive data, including our intellectual property, trade secrets or personal information of our employees, patients, customers or other business partners may be exposed to unauthorized persons or to the public. Cyber-attacks are increasing in their frequency, sophistication and intensity. Cyber-attacks could include the deployment of harmful malware, denial-of-service, social engineering and other means to affect service reliability and threaten data confidentiality, integrity and availability. Our business partners face similar risks and any security breach of their systems could adversely affect our security posture. A security breach or privacy violation that leads to disclosure or modification of or prevents access to patient information, including personally identifiable information or protected health information, could harm our reputation, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, require us to verify the correctness of database contents and otherwise subject us to litigation or other liability under laws and regulations that protect personal data, any of which could disrupt our business and/or result in increased costs or loss of revenue. Moreover, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information, trade secrets or other intellectual property. While we have invested, and continue to invest, in the protection of our data and information technology infrastructure, there can be no assurance that our efforts will prevent service interruptions, or identify breaches in our systems, that could adversely affect our business and operations and/or result in the loss of critical or sensitive information, which could result in financial, legal, business or reputational harm to us. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyber-attacks and other related breaches.

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;
- 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;
- changes in the structure of healthcare payment systems;
- 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 493,145 shares of our common stock issuable upon the exercise of warrants that were owned by the Baker Entities as of December 31, 2018, and which represent approximately 18 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 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.

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

To date, we have not paid any cash dividends on our common stock, and we do not intend to pay any dividends in the foreseeable future. Instead, we intend to retain any future earnings to fund the development and growth of our business. For this reason, the success of an investment in our common stock, if any, will depend on the appreciation of our common stock, which may not occur. There is no guarantee that our common stock will appreciate, and therefore, a holder of our common stock may not realize a return on his or her investment.

Item 1B. *Unresolved Staff Comments.*

This item is not applicable.

Item 2. *Properties.*

As of December 31, 2018, our primary facility consists of approximately 78,000 square feet of leased office space located in San Diego, California, which is leased through May 2020. We also lease a facility in Princeton, New Jersey that covers approximately 25,000 square feet of office space, which is leased through January 2025.

During the fourth quarter of 2018, we entered into a new lease agreement for the lease of approximately 67,000 square feet of office space in San Diego, California. We anticipate moving into this facility around May 2020 in connection with the expiration of the lease for our current primary facility.

Item 3. *Legal Proceedings.*

Between July 19 and August 3, 2018, following recent negative publicity about NUPLAZID, three purported Company stockholders filed putative securities class action complaints (captioned Staublein v. ACADIA Pharmaceuticals, Inc., Case No. 18-cv-01647, Stone v. ACADIA Pharmaceuticals Inc., Case No. 18-cv-01672, and Barglow v. ACADIA Pharmaceuticals Inc., Case No. 18-cv-01812) in the U.S. District Court for the Southern District of California against us and certain of our current and former 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. The complaints seek unspecified monetary damages and other relief. Several putative lead plaintiffs filed motions to consolidate the cases and to appoint a lead plaintiff. On January 3, 2019, the court consolidated the cases under Case No. 18-cv-01647 and took the lead plaintiff motions under submission. The defendants' response to the complaints is stayed pending resolution of the lead plaintiff motions. We have assessed such legal proceedings, and given the unpredictability inherent in litigation, we cannot predict the outcome of these matters. At this time, we are unable to estimate possible losses or ranges of losses that may result from such legal proceedings, and we have not accrued any amounts in connection with such legal proceedings other than ongoing attorneys' fees.

Government Investigation

In September 2018, we received a civil investigative demand ("CID") from the Department of Justice ("DOJ") 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.

Item 4. ***Mine Safety Disclosures.***

This item is not applicable.

PART II

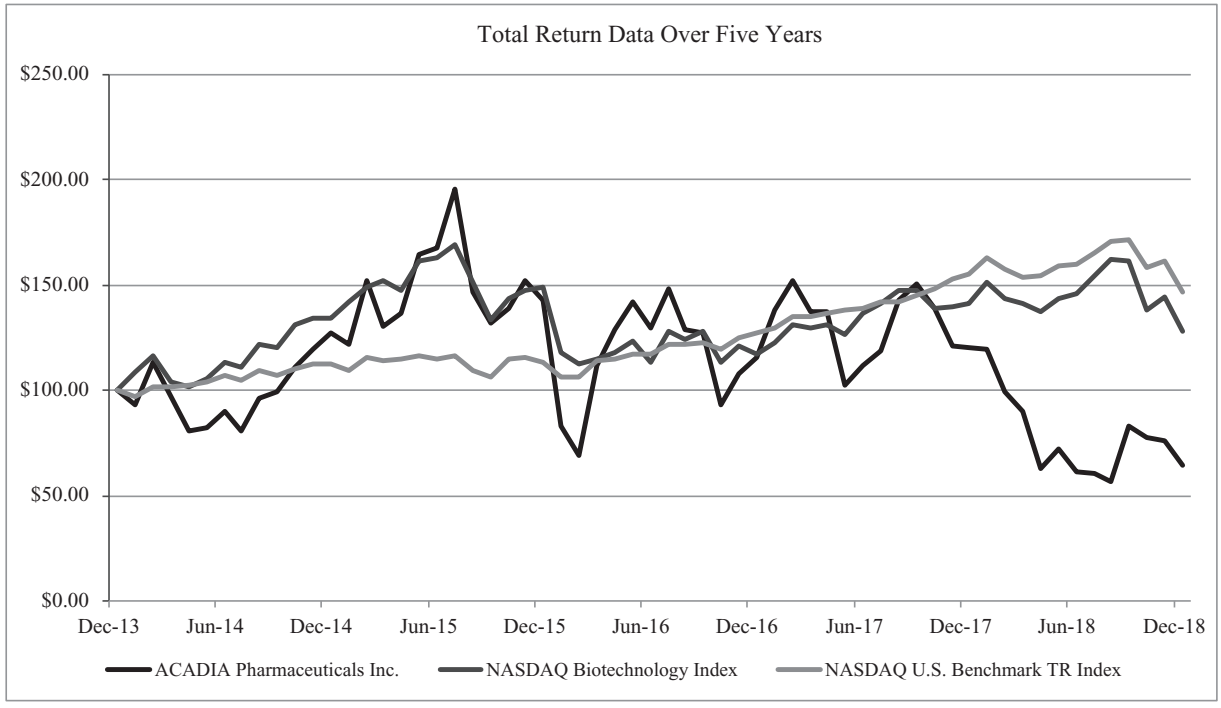
Item 5. ***Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.***

Our common stock is traded on the Nasdaq Global Select Market under the symbol "ACAD".

As of January 31, 2019, there were 143,882,381 shares of common stock outstanding held by approximately 30 stockholders of record. Many stockholders hold their shares in street name and we believe that there are approximately 36,000 beneficial owners of our common stock.

Performance Graph

The following graph shows a comparison of the total cumulative returns of an investment of $100 in cash from December 31, 2013 through December 31, 2018 in (i) our common stock, (ii) the Nasdaq Biotechnology Index, and (iii) the Nasdaq U.S. Benchmark TR Index. The comparisons in the graph are required by the SEC and are not intended to forecast or be indicative of the possible future performance of our common stock. The graph assumes that all dividends have been reinvested (to date, we have not declared any dividends).



Item 6. ***Selected Financial Data.***

The following data has been derived from our audited financial statements, including the consolidated balance sheets at December 31, 2018 and 2017 and the related consolidated statements of operations for each of the three years ended December 31, 2018 and related notes appearing elsewhere in this report. The consolidated statement of operations data for the years ended December 31, 2015 and 2014 and the consolidated balance sheet data as of December 31, 2016, 2015 and 2014 are derived from our audited consolidated financial statements that are not included in this report. You should read the selected financial data set forth below in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and related notes included elsewhere in this report.

	Years Ended December 31,				
	2018	2017	2016	2015	2014
	(in thousands, except per share amounts)				
Consolidated Statement of Operations Data:					
Revenues:					
Product sales, net	$ 223,807	$ 124,901	$ 17,327	$ —	$ —
Collaborative revenue	—	—	4	61	120
Total revenues	223,807	124,901	17,331	61	120
Operating expenses:					
Cost of product sales	12,377	9,077	3,075	—	—
License fees and royalties	5,953	3,983	1,331	2,500	—
Research and development	187,163	149,189	99,284	73,869	60,602
Selling, general and administrative	265,758	255,062	186,456	88,304	32,748
Total operating expenses	471,251	417,311	290,146	164,673	93,350
Loss from operations	(247,444)	(292,410)	(272,815)	(164,612)	(93,230)
Interest income, net	5,348	4,126	2,763	499	755
Other expense	(1,840)	—	—	—	—
Loss before income taxes	(243,936)	(288,284)	(270,052)	(164,113)	(92,475)
Income tax expense	1,256	1,119	1,341	330	—
Net loss	$(245,192)	$(289,403)	$(271,393)	$(164,443)	$(92,475)
Net loss per common share, basic and diluted	$ (1.94)	$ (2.36)	$ (2.34)	$ (1.63)	$ (0.95)
Weighted average common shares outstanding, basic and diluted	126,583	122,600	115,858	100,630	97,248

	At December 31,				
	2018	2017	2016	2015	2014
	(in thousands)				
Consolidated Balance Sheet Data:					
Cash, cash equivalents and investment securities	$ 473,520	$ 341,342	$ 529,036	$ 215,132	$ 322,486
Working capital	466,541	324,447	505,312	197,087	308,784
Total assets	540,202	384,506	561,153	221,896	325,458
Total stockholders' equity	479,079	335,285	518,411	199,762	309,489

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

The following discussion and analysis of our consolidated financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes included elsewhere in this report. Past operating results are not necessarily indicative of results that may occur in future periods. This discussion contains forward-looking statements, which involve a number of risks and uncertainties. Such forward-looking statements include statements about the benefits to be derived from NUPLAZID® (pimavanserin) and from our drug candidates, 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, 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 other statements that are not historical facts, including statements which may be preceded by the words "believes," "expects," "hopes," "may," "will," "plans," "intends," "estimates," "could," "should," "would," "continues," "seeks," "aims," "projects," "predicts," "pro forma," "anticipates," "potential" or similar words. In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain. For forward-looking statements, we claim the protection of the Private Securities Litigation Reform Act of 1995. Readers of this report are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date on which they are made. We undertake no obligation to update or revise publicly any forward-looking statements. Forward-looking statements are not guarantees of performance. Actual results or events may differ materially from those anticipated in our forward-looking statements as a result of various factors, including those set forth under the section captioned "Risk Factors" elsewhere in this report. Information in the following discussion for a yearly period means for the year ended December 31 of the indicated year.

Overview

Background

We are a biopharmaceutical company focused on the development and commercialization of innovative medicines 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. 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 and a 10 mg NUPLAZID tablet.

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. 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.

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 weight gain observed or impact on motor function. In February 2019, we conducted an End-of-Phase 2 Meeting with the FDA and we plan to initiate a Phase 3 program for pimavanserin as an adjunctive treatment for MDD in the first half of 2019.

We also believe schizophrenia represents a disease with multiple unmet or ill-served needs and we are currently exploring the utility of pimavanserin in this area. In the fourth quarter of 2016, we initiated two studies evaluating the adjunctive use of pimavanserin in patients with schizophrenia. ENHANCE 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 study in mid-2019. ADVANCE is a Phase 2 study evaluating pimavanserin for adjunctive treatment in patients with negative symptoms of schizophrenia.

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 predominantly 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. 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.

During 2015, we licensed worldwide intellectual property rights related to pimavanserin in certain indications to ACADIA Pharmaceuticals GmbH, our wholly-owned Swiss subsidiary. Our active pharmaceutical ingredient, or API, for our NUPLAZID (pimavanserin) program has been manufactured in Switzerland for over 10 years and we anticipate continuing to manufacture our API in Switzerland. ACADIA Pharmaceuticals GmbH manages the worldwide supply chain of pimavanserin API. We believe the establishment of ACADIA Pharmaceuticals GmbH, as well as the licensing of worldwide intellectual property rights for pimavanserin, will allow us to build a platform for long-term operational and financial efficiencies.

We have incurred substantial operating losses since our inception due in large part to expenditures for our research and development activities and more recently for our sales and marketing activities related to the commercialization of NUPLAZID. As of December 31, 2018, we had an accumulated deficit of $1.5 billion. We expect to continue to incur operating losses for at least the next few years as we advance our programs and incur significant development and commercialization costs.

Financial Operations Overview

Product and Collaborative Revenues

Net product sales consist of sales of NUPLAZID, our first and only commercial product to date. The FDA approved NUPLAZID in April 2016 and we launched the product in the United States in May 2016. Prior to the generation of revenue from NUPLAZID, our revenues had been generated substantially from payments under our collaboration agreements.

Cost of Product Sales

Cost of product sales consists of third-party manufacturing costs, freight, and indirect overhead costs associated with sales of NUPLAZID. Cost of product sales may also include period costs related to certain inventory manufacturing services, excess or obsolete inventory adjustment charges, unabsorbed manufacturing and overhead costs, and manufacturing variances.

License Fees and Royalties

License fees and royalties consist of milestone payments expensed or capitalized and subsequently amortized under our 2006 license agreement with the Ipsen Group. License fees and royalties also include royalties of two percent due to the Ipsen Group based upon net sales of NUPLAZID.

Research and Development Expenses

Our research and development expenses have consisted primarily of fees paid to external service providers, salaries and related personnel expenses, facilities and equipment expenses, and other costs incurred related to pre-commercial product candidates. We charge all research and development expenses to operations as incurred. Our research and development activities have primarily focused on NUPLAZID (pimavanserin) which was approved by the FDA for the treatment of hallucinations and delusions associated with PD Psychosis in April 2016. We currently are responsible for all costs incurred in the ongoing development of pimavanserin and we expect to continue to make substantial investments in clinical studies of pimavanserin for indications other than PD Psychosis, including dementia-related psychosis, schizophrenia and depression. Additionally, in connection with the FDA approval of

NUPLAZID, we committed to conduct post-marketing studies, including a randomized, placebo-controlled withdrawal study in PD Psychosis patients treated with NUPLAZID and randomized, placebo-controlled eight-week studies in predominantly frail and elderly patients that would add to the NUPLAZID safety database by exposing an aggregate of at least 500 patients to NUPLAZID. We will be responsible for all costs incurred for these post-marketing studies. We expect to incur increased research and development expenses as a result of our development of trofinetide under the exclusive North American license granted to us by Neuren Pharmaceuticals, including the costs of the planned Phase 3 randomized, double-blind placebo-controlled study evaluating trofinetide in girls with Rett syndrome. We currently are responsible for all costs incurred in the development of trofinetide, as well as milestone payments subject to achievement of development milestones.

We use external service providers to manufacture our product candidates and for the majority of the services performed in connection with the preclinical and clinical development of pimavanserin. Historically, we have used our internal research and development resources, including our employees and discovery infrastructure, across several projects and many of our costs have not been attributable to a specific project. Accordingly, we have not reported our internal research and development costs on a project basis. To the extent that external expenses are not attributable to a specific project, they are included in other programs. The following table summarizes our research and development expenses for the years ended December 31, 2018, 2017, and 2016 (in thousands):

	Years Ended December 31,		
	2018	2017	2016
Costs of external service providers:			
NUPLAZID (pimavanserin)	$ 94,697	$ 83,402	$ 53,622
Trofinetide	12,083	—	—
Other programs	5,207	505	518
Subtotal	111,987	83,907	54,140
Internal costs	43,138	38,797	27,094
Stock-based compensation	32,038	26,485	18,050
Total research and development	$ 187,163	$ 149,189	$ 99,284

Although NUPLAZID was approved by the FDA for the treatment of hallucinations and delusions associated with PD Psychosis, at this time, due to the risks inherent in clinical development, we are unable to estimate with certainty the costs we will incur for the ongoing development of pimavanserin in additional indications, including those within dementia-related psychosis, schizophrenia and depression, and the development of trofinetide. Due to these same factors, we are unable to determine with any certainty the anticipated completion dates for our current research and development programs. Clinical development and regulatory approval timelines, probability of success, and development costs vary widely. While our current development efforts are primarily focused on advancing the development of pimavanserin in additional indications other than PD Psychosis, we anticipate that we will make determinations as to which programs to pursue and how much funding to direct to each program on an ongoing basis in response to the scientific and clinical success of each product candidate, as well as an ongoing assessment of the commercial potential of each opportunity and our financial position. We cannot forecast with any degree of certainty which product opportunities will be subject to future collaborative or licensing arrangements, when such arrangements will be secured, if at all, and to what degree any such arrangements would affect our development plans and capital requirements. Similarly, we are unable to estimate with certainty the costs we will incur for post-marketing studies that we committed to conduct in connection with FDA approval of NUPLAZID.

We expect our research and development expenses to increase and continue to be substantial as we conduct studies pursuant to our post-marketing commitments and pursue the development of pimavanserin in additional indications other than PD Psychosis, including our studies within dementia-related psychosis, schizophrenia and depression indications and the development of trofinetide in Rett Syndrome. The lengthy process of completing clinical trials and supporting development activities and seeking regulatory approval for our product opportunities requires the expenditure of substantial resources. Any failure by us or delay in completing clinical trials, or in obtaining regulatory approvals, could cause our research and development expenses to increase and, in turn, have a material adverse effect on our results of operations.

Selling, General and Administrative Expenses

Our selling, general and administrative expenses consist of salaries and other related costs, including stock-based compensation expense, for our commercial personnel, including our specialty sales force, our medical education professionals, and our personnel serving in executive, finance, business development, and business operations functions. Also included in selling, general and administrative expenses are fees paid to external service providers to support our commercial activities associated with NUPLAZID, professional fees associated with legal and accounting services, costs associated with patents and patent applications for our intellectual property and charitable donations to independent charitable foundations that support Parkinson's disease patients

generally. We expect our selling, general and administrative expenses to increase in future periods to support commercial activities associated with NUPLAZID and our further development of pimavanserin in additional indications other than PD Psychosis.

Critical Accounting Policies and Estimates

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

Revenue Recognition

Product Sales, Net

Effective January 1, 2018, we adopted ASU 2014-09, *Revenue from Contracts with Customers (Topic 606),* and applied all the related amendments to all of the contracts using the modified-retrospective method. While results for reporting periods beginning after January 1, 2018 are presented under the new guidance, prior period amounts are not adjusted and continue to be reported under the accounting standards in effect for the prior period. The accounting policy for revenue recognition for periods prior to January 1, 2018 is described in Note 2 of the Notes to the Consolidated Financial Statements included in our Annual Report. Under Topic 606, we recognize revenue when our customer obtains control of promised goods or services, in an amount that reflects the consideration which we expect to receive in exchange for those goods or services. To determine revenue recognition for arrangements that we determine are within the scope of Topic 606, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy a performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services we transfer to the customer. At contract inception, once the contract is determined to be within the scope of Topic 606, we assess the goods or services promised within such contract, determine those that are performance obligations, and assess whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. Payment terms differ by customer, but typically range from 31 to 35 days from the date of shipment. Revenue for our product sales has not been adjusted for the effects of a financing component as we expect, at contract inception, that the period between when we transfer control of the product and when we receive payment will be one year or less. No cumulative effect adjustment to the opening balance of retained earnings was necessary upon adoption, and there is no reconciliation of our Consolidated Statements of Operations, as no revenue recognition differences were identified when comparing the revenue recognition criteria under Topic 606 to previous requirements.

Our net product sales consist of U.S. sales of NUPLAZID. NUPLAZID was approved by the FDA in April 2016 and we commenced shipments of NUPLAZID to specialty pharmacies, or SPs, and specialty distributors, or SDs, in late May 2016. SPs dispense product to a patient based on the fulfillment of a prescription and SDs sell product to government facilities, long-term care pharmacies, or in-patient hospital pharmacies. Product shipping and handling costs are included in cost of product sales.

We recognize revenue from product sales at the net sales price (the "transaction price") which includes estimates of variable consideration for which reserves are established and reflects each of these as either a reduction to the related account receivable or as an accrued liability, depending on how the amount payable is settled. Overall, these reserves reflect our best estimates of the amount of consideration to which we are entitled based on the terms of the contract. The amount of variable consideration that is included in the transaction price may be constrained, and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from estimates, we may need to adjust our estimates, which would affect net revenue in the period of adjustment. The following represent our significant categories of sales discounts and allowances:

Distribution Fees: Distribution fees include distribution service fees paid to our SPs and SDs based on a contractually fixed percentage of the wholesale acquisition cost, or WAC, fees for data, and prompt payment discounts. Distribution fees are recorded as an offset to revenue based on contractual terms at the time revenue from the sale is recognized.

Rebates: Allowances for rebates include mandated discounts under the Medicaid Drug Rebate Program and the Medicare Part D prescription drug benefit. Rebates are amounts owed after the final dispensing of the product to a benefit plan participant and are based upon contractual agreements with, or statutory requirements pertaining to, Medicaid and Medicare benefit providers. The allowance for rebates is based on statutory discount rates and expected utilization. Our estimates for expected utilization of rebates is based on historical data received from the SPs and SDs since product launch. Rebates are generally invoiced and paid in arrears so that

the accrual balance consists of an estimate of the amount expected to be incurred for the current quarter's activity, plus an accrual balance for prior quarters' unpaid rebates.

Chargebacks: Chargebacks are discounts and fees that relate to contracts with government and other entities purchasing from the SDs at a discounted price. The SDs charge back to us the difference between the price initially paid by the SDs and the discounted price paid to the SDs by these entities. We also incur group purchasing organization fees for transactions through certain purchasing organizations. We estimate sales with these entities and accrue for anticipated chargebacks and organization fees, based on the applicable contractual terms.

Co-Payment Assistance: We offer co-payment assistance to commercially insured patients meeting certain eligibility requirements. Co-payment assistance is accrued for based on actual program participation and estimates of program redemption using data provided by third-party administrators.

Product Returns: Consistent with industry practice, we offer the SPs and SDs limited product return rights for damages, shipment errors, and expiring product; provided that the return is within a specified period around the product expiration date as set forth in the applicable individual distribution agreement. We do not allow product returns for product that has been dispensed to a patient. As we receive inventory reports from the SPs and SDs and have the ability to control the amount of product that is sold to the SPs and SDs, we are able to make a reasonable estimate of future potential product returns based on this on-hand channel inventory data and sell-through data obtained from the SPs and SDs. In arriving at our estimate, we also consider historical product returns, the underlying product demand, and industry data specific to the specialty pharmaceutical distribution industry.

Research and Development Accruals

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

Stock-Based Compensation

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

Results of Operations

Fluctuations in Operating Results

Our results of operations have fluctuated significantly from period to period in the past and are likely to continue to do so in the future. We anticipate that our quarterly and annual results of operations will be impacted for the foreseeable future by several factors, including the progress and timing of expenditures related to our commercial activities associated with NUPLAZID and the extent to which we generate revenue from product sales, our development of pimavanserin in additional indications other than PD Psychosis, our development of Trofinetide in Rett Syndrome, the progress and timing of expenditures related to studies pursuant to our post-marketing commitments, and the timing and amount of payments received pursuant to collaborations. Further, we expect our sales allowances to vary from quarter to quarter due to fluctuations in our Medicare Part D Coverage Gap liability and the volume of purchases eligible for government mandated discounts and rebates, as well as changes in discount percentages that may be impacted by potential future price increases and other factors. Due to these fluctuations, we believe that the period-to-period comparisons of our operating results are not a good indication of our future performance.

Comparison of the Years Ended December 31, 2018 and 2017

Product Sales, Net

Net product sales, comprised of NUPLAZID, were $223.8 million and $124.9 million in 2018 and 2017, respectively. Net product sales for the year ended 2018 increased as compared to the year ended 2017 primarily due to growth in NUPLAZID unit sales of approximately 43% in 2018 compared to 2017. Also contributing to the increase was a higher average gross selling price of NUPLAZID in 2018 as compared to 2017.

The following table provides a summary of activity with respect to our sales allowances and accruals for the year ended December 31, 2018 (in thousands):

	Distribution Fees, Discounts & Chargebacks	Co-Pay Assistance	Rebates, Data Fees & Returns	Total
Balance at December 31, 2017	$ 246	$ (56)	$ 3,401	$ 3,591
Provision related to current period sales	24,613	1,266	18,673	44,552
Credits/payments for current period sales	(22,773)	(1,236)	(12,824)	(36,833)
Credits/payments for prior period sales	(246)	56	(3,401)	(3,591)
Balance at December 31, 2018	$ 1,840	$ 30	$ 5,849	$ 7,719

Cost of Product Sales

Cost of product sales was $12.4 million and $9.1 million in 2018 and 2017, respectively, or approximately 6% and 7% of net product sales. The cost of product sales as a percentage of net sales decreased during 2018 as compared to 2017 due primarily to higher manufacturing levels, resulting in higher inventory cost absorption, and increased sales volume at a higher average gross selling price in 2018, partially offset by charges of $2.7 million in 2018 to reduce certain finished goods and work in process inventory to its net realizable value. Product sold during 2018 and 2017 was manufactured with raw material that was previously charged to research and development expense prior to FDA approval of NUPLAZID. This zero cost raw material did not materially impact our cost of product sales and related product gross margins in 2018 and 2017.

License Fees and Royalties

License fees and royalties were $6.0 million and $4.0 million in 2018 and 2017, respectively, and include amortization related to the milestone paid to the Ipsen Group upon FDA approval of NUPLAZID in 2016 and royalties due to the Ipsen Group of two percent of net sales of NUPLAZID. The increase in license fees and royalties was due to the increase in sales volume during 2018.

Research and Development Expenses

Research and development expenses increased to $187.2 million in 2018, including $32.0 million in stock-based compensation, from $149.2 million in 2017, including $26.5 million in stock-based compensation. The increase in research and development expense was due to an increase of $28.1 million in external service costs and an increase of $9.9 million in personnel and related costs, including an increase of $5.5 million in stock compensation expense. The increase in external service costs was primarily due to increased clinical study costs, as we continue to invest in our life cycle management programs for pimavanserin, as well as an upfront payment of $10.0 million to Neuren Pharmaceuticals related to our in-license of trofinetide.

Selling, General and Administrative Expenses

Selling, general and administrative expenses increased to $265.8 million in 2018, including $45.7 million in stock-based compensation, from $255.1 million in 2017, including $45.3 million in stock-based compensation. The increase in selling, general and administrative expenses was due to an increase of $3.6 million in external service costs and an increase of $7.1 million in personnel and related costs, including an increase of $0.3 million in stock compensation expense. The increase in external service costs was primarily due to an increase in marketing expense related to our direct-to-consumer advertising campaign. The increase in personnel and related costs was largely due to an increase in costs associated with our specialty sales force in long-term care that was expanded in the first half of 2017.

Comparison of the Years Ended December 31, 2017 and 2016

Product Sales, Net

Net product sales, comprised of NUPLAZID, which we launched in May 2016, were $124.9 million and $17.3 million in 2017 and 2016, respectively. Net product sales for the year ended 2017 increased as compared to the year ended 2016 due to continued growth in sales of NUPLAZID since its launch in mid-2016 and a higher average sales price for NUPLAZID in 2017 as compared to 2016.

The following table provides a summary of activity with respect to our sales allowances and accruals for the year ended December 31, 2017 (in thousands):

	Distribution Fees, Discounts & Chargebacks	Co-Pay Assistance	Rebates, Data Fees & Returns	Total
Balance at December 31, 2016	$ 201	$ (1)	$ 1,799	$ 1,999
Provision related to current period sales	12,837	964	9,941	23,742
Credits/payments for current period sales	(12,591)	(1,020)	(6,540)	(20,151)
Credits/payments for prior period sales	(201)	1	(1,799)	(1,999)
Balance at December 31, 2017	$ 246	$ (56)	$ 3,401	$ 3,591

Cost of Product Sales

Cost of product sales was $9.1 million and $3.1 million in 2017 and 2016, respectively, or approximately 7% and 18% of net product sales. Costs of sales increased for the year ended December 31, 2017 as compared to 2016 due to lower manufacturing levels, resulting in lower inventory cost absorption, and greater sales volume. Additionally, with the launch of NUPLAZID in mid-2016, costs of sales were not incurred for the entire fiscal year in 2016. The cost of product sales as a percentage of net sales decreased during 2017 as compared to 2016 due primarily to the increased sales volume in 2017, partially offset by a charge of $0.7 million in 2017 to reduce certain finished goods inventory to its net realizable value. Product sold during 2017 and 2016 was manufactured with raw material that was previously charged to research and development expense prior to FDA approval of NUPLAZID. This zero cost raw material did not materially impact our cost of product sales and related product gross margins in 2017 and 2016.

License Fees and Royalties

License fees and royalties were $4.0 million and $1.3 million in 2017 and 2016, respectively, and include amortization related to the milestone paid to the Ipsen Group upon FDA approval of NUPLAZID in 2016 and royalties due to the Ipsen Group of two percent of net sales of NUPLAZID. The increase in license fees and royalties was due to the increase in sales volume during 2017.

Research and Development Expenses

Research and development expenses increased to $149.2 million in 2017, including $26.5 million in stock-based compensation, from $99.3 million in 2016, including $18.1 million in stock-based compensation. The increase in research and development expense was due to an increase of $29.8 million in external service costs and an increase of $20.1 million in personnel and related costs, including stock compensation expense, associated with our expanded research and development organization. The increase in external service costs was primarily due to increased clinical costs associated with the development of pimavanserin in indications other than PD Psychosis, including Alzheimer's disease, dementia-related psychosis, schizophrenia, and depression.

Selling, General and Administrative Expenses

Selling, general and administrative expenses increased to $255.1 million in 2017, including $45.3 million in stock-based compensation, from $186.5 million in 2016, including $36.0 million in stock-based compensation. The increase in selling, general and administrative expenses was due to an increase of $36.4 million in external service costs and an increase of $32.2 million in personnel and related costs, including stock compensation expense. The increase in external service costs was primarily due to additional charitable contributions to independent charitable foundations that support Parkinson's disease patients generally made during the year ended December 31, 2017 compared to the year ended December 31, 2016, as well as an increase in advertising expense related to our direct-to-consumer advertising campaign. The increase in personnel and related costs was largely due to costs associated with our specialty sales force that we hired in the second quarter of 2016 and further expanded in the first half of 2017.

Liquidity and Capital Resources

We have funded our operations primarily through sales of our equity securities, payments received under our collaboration agreements, debt financings, interest income, and, since 2016, with revenues from sales of NUPLAZID. In November 2018, we raised net proceeds of approximately $298.5 million in a follow-on public offering of our common stock. In January and August 2016, we raised total net proceeds of approximately $497.5 million in follow-on public offerings of our common stock, and in 2014 we raised net proceeds of $196.8 million in a public offering of our common stock. We anticipate that the level of cash used in our operations will increase in future periods in order to fund our ongoing and planned commercial activities for NUPLAZID, our ongoing and planned development activities for pimavanserin in additional indications other than PD Psychosis, studies to be conducted pursuant to our post-marketing commitments and our planned development activities for trofinetide for the treatment of Rett syndrome. We expect that our cash, cash equivalents, and investment securities will be sufficient to fund our planned operations through at least the next twelve months.

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

- the progress in, and the costs of, our ongoing and planned development activities for pimavanserin and trofinetide, 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 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;
- 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 PD Psychosis, or from trofinetide and 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;
- 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;
- the costs involved in filing, prosecuting, enforcing and defending patent claims and other intellectual property rights;
- the costs of securing manufacturing arrangements for clinical or commercial production of NUPLAZID or other product candidates; and
- the costs associated with litigation, including the costs incurred in defending against 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, public or private sales of our securities, debt financings, strategic collaborations, 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.

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

At December 31, 2018, we had $473.5 million in cash, cash equivalents, and investment securities, compared to $341.3 million at December 31, 2017. This $132.2 million increase in cash, cash equivalents, and investment securities during 2018 was primarily due to proceeds from our follow-on public offering in November 2018, partially offset by our cash used in operations. Net cash used in operating activities decreased to $167.5 million in 2018 compared to $217.8 million in 2017 and $208.4 million in 2016. The decrease in net cash used in operating activities in 2018 relative to 2017 was due to an increase in our net revenues, partially offset by additional clinical study activities, including a $10.0 million upfront license payment to Neuren Pharmaceuticals, and additional marketing costs related to our direct-to-consumer advertising campaign. The increase in net cash used in operating activities in 2017 relative to 2016 was primarily due to expansion of our research and development activities and additional costs to support the commercialization of NUPLAZID.

Net cash used in investing activities totaled $71.5 million in 2018 compared to net cash provided by investing activities of $92.5 million in 2017 and net cash used in investing activities of $261.9 million in 2016. Net cash used in investing activities in 2018 compared to the net cash provided by investing activities in 2017 was primarily due to a decrease in maturities of investment securities attributable to cash used to fund operations. Net cash provided by investing activities in 2017 compared to the net cash used in investing activities in 2016 was primarily due to a decrease in purchases of investment securities attributable to cash used to fund operations.

Net cash provided by financing activities increased to $306.6 million in 2018 compared to $31.2 million in 2017 and decreased compared to $533.8 million in 2016. The increase in net cash provided by financing activities in 2018 relative to 2017 was primarily attributable to the November 2018 follow-on public offering that contributed approximately $298.5 million in total net proceeds in 2018, with no comparable offering in 2017. The decrease in net cash provided by financing activities in 2017 relative to 2016 was primarily attributable to the January and August 2016 follow-on public offerings that contributed approximately $497.5 million in total net proceeds in 2016, with no comparable offerings in 2017.

Contractual Obligations

The following is a summary of our long-term contractual obligations as of December 31, 2018 (in thousands):

	Total	Less than 1 Year	1-3 Years	3-5 Years	More than 5 Years
Operating leases	$ 59,276	$ 3,287	$ 6,316	$ 10,990	$ 38,683
Other long-term contractual obligations	9,002	1,483	4,760	2,759	—
Total	$ 68,278	$ 4,770	$ 11,076	$ 13,749	$ 38,683

In addition to operating leases, we enter into certain other long-term commitments for goods and services that are outstanding for periods greater than one year. To the extent these long-term commitments are noncancelable, they are reflected in the above table. We also enter into short-term agreements with various vendors and suppliers of goods and services in the normal course of operations through purchase orders or other documentation, or that are undocumented except for an invoice. Such short-term agreements are generally outstanding for periods less than a year and are settled by cash payments upon delivery of goods and services. The nature of the work being conducted under these agreements is such that, in most cases, the services may be stopped on short notice. In such event, we would not be liable for the full amount of the agreement and therefore are not reflected in the above table.

Pursuant to the terms of our 2006 license agreement with the Ipsen Group, we are required to make royalty payments based upon net sales of NUPLAZID of two percent. Royalty payments are contingent upon net product sales and accordingly these amounts are not included in the above table.

In addition, in connection with the license agreement entered into with Neuren, we have committed to milestone payments of up to $455.0 million, based on the achievement of certain development and annual net sales milestones. In addition, Neuren is eligible to receive tiered, escalating, double-digit percentage royalties based on net sales. These payments are contingent upon achieving future regulatory and commercial milestones, and accordingly these amounts are not included in the above table.

Off-Balance Sheet Arrangements

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

Recent Accounting Pronouncements

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

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

Interest Rate Risk

We invest our excess cash in investment-grade, interest-bearing securities. The primary objective of our investment activities is to preserve principal and liquidity. To achieve this objective, we invest in money market funds and high quality marketable debt instruments of corporations and government sponsored enterprises with contractual maturity dates of generally less than two years. All investment securities have a credit rating of at least A3/A- or better, or P-1/A-1 or better, as determined by Moody's Investors Service or Standard & Poor's. We do not have any direct investments in auction-rate securities or securities that are collateralized by assets that include mortgages or subprime debt. If a 10 percent change in interest rates were to have occurred on December 31, 2018, this change would not have had a material effect on the fair value of our investment portfolio as of that date.

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

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

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

None.

Item 9A. ***Controls and Procedures.***

Disclosure Controls and Procedures

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

As of December 31, 2018, we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer, of the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended. Based on this evaluation, our Chief Executive Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2018.

Management's Report on Internal Control Over Financial Reporting

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

financial statements for external purposes in accordance with accounting principles generally accepted in the United States of America.

As of December 31, 2018, our management assessed the effectiveness of our internal control over financial reporting using the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework (2013). Based on this assessment, management, under the supervision and with the participation of our Chief Executive Officer, concluded that, as of December 31, 2018, our internal control over financial reporting was effective based on those criteria.

The effectiveness of our internal control over financial reporting as of December 31, 2018 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in its report, which is included herein.

Changes in Internal Control Over Financial Reporting

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

Report of Independent Registered Public Accounting Firm

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

Opinion on Internal Control Over Financial Reporting

We have audited ACADIA Pharmaceuticals Inc.'s internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework) (the COSO criteria). In our opinion, ACADIA Pharmaceuticals Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of ACADIA Pharmaceuticals Inc. as of December 31, 2018 and 2017, the related consolidated statements of operations, comprehensive loss, cash flows and stockholders' equity for each of the three years in the period ended December 31, 2018, and the related notes and the financial statement schedule listed in the Index at Item 15(a)2 and our report dated February 26, 2019 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

San Diego, California
February 26, 2019

Item 9B. ***Other Information***

None.

PART III

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

The information required by this Item and not set forth below will be set forth in the section headed "—Election of Directors" and "Information Regarding the Board of Directors and Corporate Governance" in our definitive Proxy Statement for our 2019 Annual Meeting of Stockholders to be filed with the SEC by April 30, 2019 (our "Proxy Statement") and is incorporated in this report by reference.

We have adopted a code of ethics for directors, officers (including our principal executive officer, principal financial officer and principal accounting officer) and employees, known as the Code of Business Conduct and Ethics. The Code of Business Conduct and Ethics is available on our website at *http://www.acadia-pharm.com* under the Corporate Governance section of our Investors page. We will promptly disclose on our website (i) the nature of any amendment to the policy that applies to our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions and (ii) the nature of any waiver, including an implicit waiver, from a provision of the policy that is granted to one of these specified individuals, the name of such person who is granted the waiver and the date of the waiver. Stockholders may request a free copy of the Code of Business Conduct and Ethics from our compliance department c/o ACADIA Pharmaceuticals Inc., 3611 Valley Centre Drive, Suite 300, San Diego, CA 92130.

Item 11. ***Executive Compensation.***

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

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

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

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

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

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

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

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

PART IV

Item 15. Exhibits and Financial Statement Schedules.

(a) Documents filed as part of this report.

1. The following financial statements of ACADIA Pharmaceuticals Inc. and Report of Ernst & Young LLP, Independent Registered Public Accounting Firm, are included in this report:

2. List of financial statement schedules:

Schedule II – Valuation and Qualifying Accounts

Schedules not listed above have been omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

3. List of Exhibits required by Item 601 of Regulation S-K. See part (b) below.

(b) Exhibits.

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	Form of common stock certificate of the Registrant (incorporated by reference to Exhibit 4.1 to Registration Statement No. 333-52492).
4.2	Form of Amended and Restated Warrant to Purchase Common Stock (superseding the form of warrant issued to certain purchasers in a private placement on December 17, 2012).
10.1[a]	Form of Indemnity Agreement for directors and officers (incorporated by reference to Exhibit 10.1 to Registration Statement No. 333-113137).
10.2[a]	2004 Equity Incentive Plan and forms of agreement thereunder (incorporated by reference to Exhibit 10.3 to Registration Statement No. 333-113137).
10.3[a]	2010 Equity Incentive Plan, as amended (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K, filed June 15, 2017).
10.4[a]	Forms of agreement under the 2010 Equity Incentive Plan (incorporated by reference to Exhibit 10.4 to the Registrant's Annual Report on Form 10-K, filed February 29, 2016).
10.5[a]	2004 Employee Stock Purchase Plan, as amended (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K, filed June 10, 2016).
10.6[a]	Offerings under the 2004 Employee Stock Purchase Plan, as amended (incorporated by reference to Exhibit 10.6 to the Registrant's Annual Report on Form 10-K, filed February 28, 2017).
10.7[a]	Employment Agreement, dated September 1, 2015, between the Registrant and Stephen Davis (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K, filed September 3, 2015).
10.8[a]	Employment Offer Letter, dated October 28, 2015, between the Registrant and Srdjan Stankovic (incorporated by reference to Exhibit 10.10 to the Registrant's Annual Report on Form 10-K, filed February 29, 2016).

Exhibit Number	Description
10.9[a]	Employment Offer Letter, dated February 24, 2017, between the Registrant and Michael J. Yang (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q, filed May 9, 2017).
10.10[a]	Employment Offer Letter, dated July 2, 2018, between the Registrant and Austin D. Kim (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q, filed November 6, 2018).
10.11[a]	Description of Executive Officer Annual Incentive Cash Compensation Program (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K, filed March 18, 2016).
10.12[a]	Management Severance Benefit Plan (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K, filed December 15, 2015).
10.13[a]	Amended and Restated Change in Control Severance Benefit Plan (incorporated by reference to Exhibit 99.2 to the Registrant's Current Report on Form 8-K, filed December 15, 2015).
10.14[a]	Description of Outside Director Compensation Program (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q, filed August 8, 2017).
10.15[b]	Master Manufacturing Services Agreement and Product Agreement, dated August 3, 2015, by and between the Registrant and Patheon Pharmaceuticals Inc. (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q, filed November 5, 2015).
10.16[b]	First Amendment to Product Agreement, dated April 25, 2016, by and between the Registrant and Patheon Pharmaceuticals Inc. (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q, filed August 4, 2016).
10.17[b]	Second Amendment to Product Agreement, dated October 6, 2016, by and between the Registrant and Patheon Pharmaceuticals Inc. (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q, filed November 7, 2016).
10.18[b]	Third Amendment to Product Agreement, dated December 11, 2017, by and between the Registrant and Patheon Pharmaceuticals Inc (incorporated by reference to Exhibit 10.19 to the Registrant's Annual Report on Form 10-K, filed February 27, 2018.
10.19[b]	Master Services Agreement, dated December 15, 2016, by and between ACADIA Pharmaceuticals GmbH and Siegfried AG and its affiliates, and Attachment #1, Attachment #2 and Attachment #3 (incorporated by reference to Exhibit 10.20 to the Registrant's Annual Report on Form 10-K, filed February 28, 2017).
10.20[b]	Change Order #1 to Master Services Agreement Attachment #1, dated January 3, 2017, by and between ACADIA Pharmaceuticals GmbH and Siegfried AG (incorporated by reference to Exhibit 10.21 to the Registrant's Annual Report on Form 10-K, filed February 28, 2017).
10.21[b]	Attachment #4, Attachment #5 and Attachment #6, each dated May 12, 2017, to the Master Services Agreement, dated December 15, 2016, by and between ACADIA Pharmaceuticals GmbH and Siegfried AG and its affiliates (incorporated by reference to Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q, filed August 8, 2017).
10.22[b]	Commercial Supply Agreement, dated February 22, 2018, by and between the Registrant and Catalent Pharma Solutions, LLC (incorporated by reference to Exhibit 10.23 to the Registrant's Annual Report on Form 10-K, filed February 27, 2018.
10.23	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).
10.24	Assignment of Brann Intellectual Property Rights, dated January 29, 1997, by Mark R. Brann in favor of the Registrant (incorporated by reference to Exhibit 10.17 to Registration Statement No. 333-52492).
10.25[b]	License Agreement, dated November 30, 2006, by and between the Registrant and Société de Conseils, de Recherches et d'Applications Scientifiques SAS, a French corporation member of the Ipsen Group (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K, filed December 4, 2006).
10.26[b]	License Agreement, dated August 6, 2018, by and between the Registrant and Neuren Pharmaceuticals Ltd.
10.27[b]	Lease Agreement, effective October 4, 2018, by and between the Registrant and Kilroy Realty, L.P.
21.1	List of subsidiaries of the Registrant.
23.1	Consent of Independent Registered Public Accounting Firm.
24.1	Power of Attorney (see signature page hereto).
31.1	Certification of Stephen Davis, Chief Executive Officer, pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities

Exhibit Number	Description
	Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1	Certification of Stephen Davis, Chief Executive Officer, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101	The following financial statements from this Annual Report, formatted in XBRL (Extensible Business Reporting Language), are filed herewith: (i) Consolidated Balance Sheets, (ii) Consolidated Statements of Operations, (iii) Consolidated Statements of Comprehensive Loss, (iv) Consolidated Statements of Cash Flows, (v) Consolidated Statements of Stockholders' Equity, and (vi) Notes to Consolidated Financial Statements.

[a] Indicates management contract or compensatory plan or arrangement.

[b] We have requested or received confidential treatment of certain portions of this agreement, which have been omitted and filed separately with the SEC pursuant to Rule 406 under the Securities Act of 1933, as amended, or Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

SIGNATURES

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

ACADIA PHARMACEUTICALS INC.

/s/ STEPHEN DAVIS
Stephen Davis
Chief Executive Officer
(on behalf of the registrant and as the registrant's Principal Executive Officer)

Date: February 26, 2019

KNOW ALL PERSONS BY THESE PRESENTS, that each individual whose signature appears below constitutes and appoints Stephen Davis, his true and lawful attorney-in-fact and agent with full power of substitution, for him and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto and all documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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

Signature	Title	Date
/s/ STEPHEN DAVIS **Stephen Davis**	Chief Executive Officer and Director (Principal Executive and Financial Officer)	February 26, 2019
/s/ ERIC MILLER **Eric Miller**	Senior Director and Controller (Principal Accounting Officer)	February 26, 2019
/s/ STEPHEN BIGGAR **Stephen Biggar**	Chairman of the Board	February 26, 2019
/s/ JULIAN BAKER **Julian Baker**	Director	February 26, 2019
/s/ LAURA BREGE **Laura Brege**	Director	February 26, 2019
/s/ JAMES DALY **James Daly**	Director	February 26, 2019
/s/ EDMUND HARRIGAN **Edmund Harrigan**	Director	February 26, 2019
/s/ DANIEL SOLAND **Daniel Soland**	Director	February 26, 2019

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Report of Independent Registered Public Accounting Firm

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

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of ACADIA Pharmaceuticals Inc. (the Company) as of December 31, 2018 and 2017, the related consolidated statements of operations, comprehensive loss, cash flows and stockholders' equity for each of the three years in the period ended December 31, 2018, and the related notes and the financial statement schedule listed in the Index at Item 15(a)2 (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated February 26, 2019 expressed an unqualified opinion thereon.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2015.

San Diego, California
February 26, 2019

ACADIA PHARMACEUTICALS INC.
CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share amounts)

	December 31, 2018	December 31, 2017
Assets		
Cash and cash equivalents	$ 134,758	$ 69,418
Investment securities, available-for-sale	338,762	271,924
Accounts receivable, net	26,090	17,343
Interest and other receivables	1,699	1,087
Inventory	4,070	5,248
Prepaid expenses	20,727	8,457
Total current assets	526,106	373,477
Property and equipment, net	3,309	2,662
Intangible assets, net	4,062	5,538
Restricted cash	4,826	2,475
Other assets	1,899	354
Total assets	$ 540,202	$ 384,506
Liabilities and stockholders' equity		
Accounts payable	$ 3,167	$ 8,786
Accrued liabilities	56,398	40,244
Total current liabilities	59,565	49,030
Long-term liabilities	1,558	191
Total liabilities	61,123	49,221
Commitments and contingencies (Note 9)		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 5,000,000 shares authorized at December 31, 2018 and 2017; no shares issued and outstanding at December 31, 2018 and 2017	—	—
Common stock, $0.0001 par value; 225,000,000 shares authorized at December 31, 2018 and December 31, 2017; 143,853,597 shares and 124,410,552 shares issued and outstanding at December 31, 2018 and December 31, 2017, respectively	14	12
Additional paid-in capital	1,948,300	1,559,343
Accumulated deficit	(1,468,863)	(1,223,671)
Accumulated other comprehensive loss	(372)	(399)
Total stockholders' equity	479,079	335,285
Total liabilities and stockholders' equity	$ 540,202	$ 384,506

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

ACADIA PHARMACEUTICALS INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except per share amounts)

	Years Ended December 31,		
	2018	2017	2016
Revenues			
Product sales, net	$ 223,807	$ 124,901	$ 17,327
Collaborative revenue	—	—	4
Total revenues	223,807	124,901	17,331
Operating expenses			
Cost of product sales	12,377	9,077	3,075
License fees and royalties	5,953	3,983	1,331
Research and development	187,163	149,189	99,284
Selling, general and administrative	265,758	255,062	186,456
Total operating expenses	471,251	417,311	290,146
Loss from operations	(247,444)	(292,410)	(272,815)
Interest income, net	5,348	4,126	2,763
Other expense	(1,840)	—	—
Loss before income taxes	(243,936)	(288,284)	(270,052)
Income tax expense	1,256	1,119	1,341
Net loss	$ (245,192)	$ (289,403)	$ (271,393)
Net loss per common share, basic and diluted	$ (1.94)	$ (2.36)	$ (2.34)
Weighted average common shares outstanding, basic and diluted	126,583	122,600	115,858

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

ACADIA PHARMACEUTICALS INC.
CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(in thousands)

	Years Ended December 31,		
	2018	2017	2016
Net loss	$ (245,192)	$ (289,403)	$ (271,393)
Other comprehensive gain (loss):			
Unrealized gain (loss) on investment securities	24	(499)	94
Foreign currency translation adjustments	3	(6)	1
Comprehensive loss	$ (245,165)	$ (289,908)	$ (271,298)

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

ACADIA PHARMACEUTICALS INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Years Ended December 31,		
	2018	2017	2016
Cash flows from operating activities			
Net loss	$ (245,192)	$ (289,403)	$ (271,393)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation	81,564	75,532	55,265
Amortization of premiums and accretion of discounts on investment securities	(578)	(291)	89
Amortization of intangible assets	1,476	1,477	985
Loss on strategic investment	1,840	—	—
Depreciation	1,529	1,236	843
Income tax benefit from exercise of stock options	—	—	(596)
Loss on disposal of assets	88	4	5
Changes in operating assets and liabilities:			
Accounts receivable, net	(8,747)	(11,440)	(5,903)
Interest and other receivables	(612)	150	401
Inventory	1,926	(1,012)	(3,305)
Prepaid expenses and other current assets	(12,270)	(911)	(4,731)
Other assets	(236)	431	(456)
Accounts payable	(5,619)	4,874	2,240
Accrued liabilities	15,994	4,206	15,579
Deferred revenue	—	(2,644)	2,644
Long-term liabilities	1,367	34	(75)
Net cash used in operating activities	(167,470)	(217,757)	(208,408)
Cash flows from investing activities			
Purchases of investment securities	(327,914)	(478,818)	(683,355)
Maturities of investment securities	261,678	572,103	430,937
Purchases of strategic investments	(3,149)	—	—
Intangible assets	—	—	(8,000)
Proceeds from sale of property and equipment	44	—	—
Purchases of property and equipment	(2,148)	(812)	(1,506)
Net cash (used in) provided by investing activities	(71,489)	92,473	(261,924)
Cash flows from financing activities			
Proceeds from issuance of common stock, net of issuance costs	306,647	31,188	518,896
Proceeds from settlement agreement	—	—	14,320
Income tax benefit from exercise of stock options	—	—	596
Net cash provided by financing activities	306,647	31,188	533,812
Effect of exchange rate changes on cash	3	(6)	2
Net increase (decrease) in cash, cash equivalents and restricted cash	67,691	(94,102)	63,482
Cash, cash equivalents and restricted cash			
Beginning of period	71,893	165,995	102,513
End of period	$ 139,584	$ 71,893	$ 165,995
Supplemental disclosure of cash flow information:			
Cash paid for income taxes	$ 1,261	$ 1,367	$ 365
Supplemental disclosure of noncash information:			
Property and equipment purchases in accounts payable and accrued liabilities	$ 160	$ 9	$ 220
Stock-based compensation capitalized in inventory	$ (748)	$ (61)	$ 870

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

ACADIA PHARMACEUTICALS INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands, except share amounts)

	Common Stock		Additional Paid-in	Accumulated	Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Capital	Deficit	Income (Loss)	Equity
Balances at December 31, 2015	101,938,702	$ 10	$ 862,327	$ (662,586)	$ 11	$ 199,762
Issuance of common stock in public offering, net of issuance costs	17,314,523	2	497,763	—	—	497,765
Issuance of common stock from exercise of stock options	1,977,661	—	18,000	—	—	18,000
Issuance of common stock pursuant to employee stock purchase plan	136,283	—	3,131	—	—	3,131
Income tax benefit from exercise of stock options	—	—	596	—	—	596
Proceeds from settlement agreement	—	—	14,320	—	—	14,320
Net loss	—	—	—	(271,393)	—	(271,393)
Stock-based compensation	—	—	56,135	—	—	56,135
Other comprehensive income	—	—	—	—	95	95
Balances at December 31, 2016	121,367,169	$ 12	$1,452,272	$ (933,979)	$ 106	$ 518,411
Issuance of common stock from exercise of stock options	1,442,411	—	26,665	—	—	26,665
Issuance of common stock pursuant to employee stock purchase plan	192,402	—	4,522	—	—	4,522
Issuance of common stock from exercise of warrants on a net issuance basis	1,408,570	—	—	—	—	—
Net loss	—	—	—	(289,403)	—	(289,403)
Cumulative effect adjustment from adoption of ASU 2016-09	—	—	—	(289)	—	(289)
Stock-based compensation	—	—	75,884	—	—	75,884
Other comprehensive loss	—	—	—	—	(505)	(505)
Balances at December 31, 2017	124,410,552	$ 12	$1,559,343	$(1,223,671)	$ (399)	$ 335,285
Issuance of common stock in public offering, net of issuance costs	18,602,941	2	298,535	—	—	298,537
Issuance of common stock from exercise of stock options	599,529	—	4,428	—	—	4,428
Issuance of common stock pursuant to employee stock purchase plan	233,720	—	3,682	—	—	3,682
Issuance of common stock from exercise of warrants on a net issuance basis	6,855	—	—	—	—	—
Net loss	—	—	—	(245,192)	—	(245,192)
Stock-based compensation	—	—	82,312	—	—	82,312
Other comprehensive loss	—	—	—	—	27	27
Balances at December 31, 2018	143,853,597	$ 14	$1,948,300	$(1,468,863)	$ (372)	$ 479,079

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

1. Organization and Business

ACADIA Pharmaceuticals Inc. (the "Company"), based in San Diego, California, is a biopharmaceutical company focused on the development and commercialization of innovative medicines to address unmet medical needs in central nervous system disorders. The Company was originally incorporated in Vermont in 1993 as Receptor Technologies, Inc. and reincorporated in Delaware in 1997.

In April 2016, the U.S. Food and Drug Administration ("FDA") approved the Company's first drug, NUPLAZID® (pimavanserin), for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis ("PD Psychosis"). NUPLAZID became available for prescription in the United States on May 31, 2016.

2. Summary of Significant Accounting Policies

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

Principles of Consolidation

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

Use of Estimates

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

Reclassifications

Pursuant to the adoption of ASU 2016-18, *Statement of Cash Flows: Restricted Cash*, the Company is presenting restricted cash with cash and cash equivalents in the beginning-of-period and end-of-period total amounts on its Consolidated Statements of Cash Flows. This reclassification reduced the Company's previously stated net cash used in operations and net decrease in cash and cash equivalents for the year ended December 31, 2017 by $0.1 million. The reclassification had no impact on the Company's balance sheets as previously reported. The following table provides a reconciliation of cash, cash equivalents and restricted cash reported in the consolidated balance sheets that sum to the total of the same such amounts shown in the Consolidated Statements of Cash Flows (in thousands).

	Twelve Months Ended December 31, 2018		Twelve Months Ended December 31, 2017		Twelve Months Ended December 31, 2016	
	Beginning of period	End of period	Beginning of period	End of period	Beginning of period	End of period
Cash and cash equivalents	$ 69,418	$134,758	$163,620	$ 69,418	$102,138	$163,620
Restricted cash	2,475	4,826	2,375	2,475	375	2,375
Total cash, cash equivalents and restricted cash shown in the statements of cash flows	$ 71,893	$139,584	$165,995	$ 71,893	$102,513	$165,995

Cash and Cash Equivalents

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

Investment Securities

The Company has classified all of its investment securities as available-for-sale as the sale of such securities may be required prior to maturity to implement management strategies, and accordingly, carries these investments at fair value. Unrealized gains and losses, if any, are reported as a separate component of stockholders' equity. The cost of investment securities classified as available-for-sale is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion are included in interest income. Realized gains and losses, if any, are also included in interest income. The cost of securities sold is based on the specific identification method.

Fair Value of Financial Instruments

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

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

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

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

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

Accounts Receivable

Accounts receivable are recorded net of customer allowances for distribution fees, prompt payment discounts, chargebacks, and doubtful accounts. Allowances for distribution fees, prompt payment discounts and chargebacks are based on contractual terms. The Company estimates the allowance for doubtful accounts based on existing contractual payment terms, actual payment patterns of its customers and individual customer circumstances. At December 31, 2018, the Company determined that an allowance for doubtful accounts was not required. During the year ended December 31, 2018, the Company wrote off less than $0.1 million. No accounts were written off during the other periods presented.

Inventory

Inventory, consisting of raw material, work in process, and finished goods, is stated at the lower of cost or estimated net realizable value. The Company uses a combination of standard and actual costing methodologies to determine the cost basis for its inventories which approximates actual costs. Inventory is valued on a first-in, first-out basis and includes third-party manufacturing costs, freight, and indirect overhead costs. The Company capitalizes inventory costs associated with its products upon regulatory approval when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized; otherwise, such costs are expensed. Prior to FDA approval of NUPLAZID in April 2016, all costs related to the manufacturing of NUPLAZID were charged to research and development expense in the period incurred. The Company reduces its inventory to net realizable value for potentially excess, dated or obsolete inventory based on an analysis of forecasted demand compared to quantities on hand and any firm purchase orders, as well as product shelf life. During 2018 and 2017, the Company recorded charges of $2.7 million and $0.7 million, respectively, to reduce certain finished goods and work in process inventory to its net realizable value. No such charges were recorded in 2016.

Property and Equipment

Property and equipment are recorded at cost and depreciated over their estimated useful lives using the straight-line method. Leasehold improvements are amortized over the shorter of their estimated useful lives or the term of the lease by use of the straight-line method. Construction-in-process reflects amounts incurred for property, equipment or improvements that have not been placed in service. Maintenance and repair costs are expensed as incurred. When assets are retired or sold, the assets and accumulated depreciation are removed from the respective accounts and any gain or loss is recognized.

Estimated useful lives by major asset category are as follows:

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

Impairment of Long-Lived Assets

The Company reviews its long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by a comparison of the carrying amount of an asset to estimated undiscounted future cash flows expected to be generated by the asset. If the carrying amount of an asset exceeds its estimated future cash flows, an impairment charge is recognized by the amount by which the carrying amount of the asset exceeds the fair value of the asset. Through December 31, 2018, no such impairment losses have been recorded by the Company.

License Fees and Royalties

The Company expenses amounts paid to acquire licenses associated with products under development when the ultimate recoverability of the amounts paid is uncertain and the technology has no alternative future use when acquired. Acquisitions of technology licenses are charged to expense or capitalized based upon management's assessment regarding the ultimate recoverability of the amounts paid and the potential for alternative future use. The Company has determined that technological feasibility for its product candidates is reached when the requisite regulatory approvals are obtained to make the product available for sale.

In connection with the FDA approval of NUPLAZID in April 2016, the Company made a one-time milestone payment of $8.0 million pursuant to its 2006 license agreement with the Ipsen Group in which the Company licensed certain intellectual property rights that complement its patent portfolio for its serotonin platform, including NUPLAZID. The Company capitalized the $8.0 million payment as an intangible asset and is amortizing the asset on a straight-line basis over the estimated useful life of the licensed patents through the second half of 2021. The Company recorded amortization expense related to its intangible asset of $1.5 million, $1.5 million and $1.0 million for the years ended December 31, 2018, 2017 and 2016, respectively. As of December 31, 2018, estimated future amortization expense related to the Company's intangible asset was $1.5 million for each of 2019 and 2020, and $1.0 million for 2021.

Royalties incurred in connection with the Company's license agreement with the Ipsen Group, as disclosed in Note 9, are expensed to license fees and royalties as revenue from product sales is recognized.

Advertising Expense

In connection with the FDA approval and commercial launch of NUPLAZID in 2016, the Company began to incur advertising costs. Advertising costs are expensed when services are performed or goods are delivered. The Company incurred $39.8 million, $15.6 million and $1.6 million in advertising costs in 2018, 2017 and 2016, respectively, related to its marketed product, NUPLAZID. No advertising costs were capitalized as prepaid expenses at December 31, 2018 or 2017.

Revenue Recognition

Product Sales, Net

Effective January 1, 2018, the Company adopted ASU 2014-09, *Revenue from Contracts with Customers (Topic 606),* and applied all the related amendments to all of the contracts using the modified-retrospective method. While results for reporting periods beginning after January 1, 2018 are presented under the new guidance, prior period amounts are not adjusted and continue to be reported under the accounting standards in effect for the prior period. The accounting policy for revenue recognition for periods prior to January 1, 2018 is described in Note 2 of the Notes to the Consolidated Financial Statements included in the Company's 2017 Annual Report. Under Topic 606, the Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the Company expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of Topic 606, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies a performance obligation. The Company only applies the five-step model to contracts

when it is probable that the Company will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of Topic 606, the Company assesses the goods or services promised within each contract, determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied. Payment terms differ by customer, but typically range from 31 to 35 days from the date of shipment. Revenue for the Company's product sales has not been adjusted for the effects of a financing component as the Company expects, at contract inception, that the period between when the Company transfers control of the product and when the Company receives payment will be one year or less. No cumulative effect adjustment to the opening balance of retained earnings was necessary upon adoption, and there is no reconciliation of the Company's Consolidated Statements of Operations, as no revenue recognition differences were identified when comparing the revenue recognition criteria under Topic 606 to previous requirements.

The Company's net product sales consist of U.S. sales of NUPLAZID. NUPLAZID was approved by the FDA in April 2016 and the Company commenced shipments of NUPLAZID to specialty pharmacies ("SPs") and specialty distributors ("SDs") in late May 2016. SPs dispense product to a patient based on the fulfillment of a prescription and SDs sell product to government facilities, long-term care pharmacies, or in-patient hospital pharmacies. Product shipping and handling costs are included in cost of product sales.

The Company recognizes revenue from product sales at the net sales price (the "transaction price") which includes estimates of variable consideration for which reserves are established and reflects each of these as either a reduction to the related account receivable or as an accrued liability, depending on how the amount payable is settled. Overall, these reserves reflect the Company's best estimates of the amount of consideration to which the Company is entitled based on the terms of the contract. The amount of variable consideration that is included in the transaction price may be constrained, and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results in the future vary from estimates, the Company may need to adjust its estimates, which would affect net revenue in the period of adjustment. The following are the Company's significant categories of sales discounts and allowances:

Distribution Fees: Distribution fees include distribution service fees paid to the SPs and SDs based on a contractually fixed percentage of the wholesale acquisition cost ("WAC"), fees for data, and prompt payment discounts. Distribution fees are recorded as an offset to revenue based on contractual terms at the time revenue from the sale is recognized.

Rebates: Allowances for rebates include mandated discounts under the Medicaid Drug Rebate Program and the Medicare Part D prescription drug benefit. Rebates are amounts owed after the final dispensing of the product to a benefit plan participant and are based upon contractual agreements with, or statutory requirements pertaining to, Medicaid and Medicare benefit providers. The allowance for rebates is based on statutory discount rates and expected utilization. The Company's estimates for expected utilization of rebates is based on historical data received from the SPs and SDs since product launch. Rebates are generally invoiced and paid in arrears so that the accrual balance consists of an estimate of the amount expected to be incurred for the current quarter's activity, plus an accrual balance for prior quarters' unpaid rebates.

Chargebacks: Chargebacks are discounts and fees that relate to contracts with government and other entities purchasing from the SDs at a discounted price. The SDs charge back to the Company the difference between the price initially paid by the SDs and the discounted price paid to the SDs by these entities. The Company also incurs group purchasing organization fees for transactions through certain purchasing organizations. The Company estimates sales with these entities and accrues for anticipated chargebacks and organization fees, based on the applicable contractual terms.

Co-Payment Assistance: The Company offers co-payment assistance to commercially insured patients meeting certain eligibility requirements. Co-payment assistance is accrued for based on actual program participation and estimates of program redemption using data provided by third-party administrators.

Product Returns: Consistent with industry practice, the Company offers the SPs and SDs limited product return rights for damages, shipment errors, and expiring product; provided that the return is within a specified period around the product expiration date as set forth in the applicable individual distribution agreement. The Company does not allow product returns for product that has been dispensed to a patient. As the Company receives inventory reports from the SPs and SDs and has the ability to control the amount of product that is sold to the SPs and SDs, it is able to make a reasonable estimate of future potential product returns based on this on-hand channel inventory data and sell-through data obtained from the SPs and SDs. In arriving at its estimate for product

returns, the Company also considers historical product returns, the underlying product demand, and industry data specific to the specialty pharmaceutical distribution industry.

Research and Development Expenses

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

Concentration Risk

Financial instruments, which potentially subject the Company to concentrations of credit risk, principally consist of cash, cash equivalents, investment securities, accounts receivable, and restricted cash. The Company invests its excess cash primarily in money market funds, U.S. Treasury notes, and high quality, marketable debt instruments of corporations and government sponsored enterprises in accordance with the Company's investment policy. The Company's investment policy defines allowable investments and establishes guidelines relating to credit quality, diversification, and maturities of its investments to preserve principal and maintain liquidity. All investment securities have a credit rating of at least A3/A- or better, or P-1/A-1 or better, as determined by Moody's Investors Service or Standard & Poor's. Further, the Company specifies credit quality standards for its customers that are designed to limit the Company's credit exposure to any single party.

The Company does not currently have any of its own manufacturing facilities, and therefore it depends on an outsourced manufacturing strategy for the production of NUPLAZID for commercial use and for the production of its product candidates for clinical trials. The Company has contracts in place with two third-party manufacturers of commercial drug product and one third-party manufacturer of drug substance that is approved for the production of NUPLAZID active pharmaceutical ingredient ("API"). Although there are potential sources of supply other than the Company's existing suppliers, any new supplier would be required to qualify under applicable regulatory requirements.

The Company has entered into distribution agreements with a limited number of SPs and SDs, and all of the Company's product sales are to these customers. For the year ended December 31, 2018, the Company's four largest customers represented approximately 85% of the Company's product revenue and 84% of the Company's accounts receivable balance at December 31, 2018. For the year ended December 31, 2017, the Company's four largest customers represented approximately 89% of the Company's product revenue and 87% of the Company's accounts receivable balance at December 31, 2017. For the year ended December 31, 2016, the Company's four largest customers represented approximately 93% of the Company's product revenue and 91% of the Company's accounts receivable balance at December 31, 2016.

Stock-Based Compensation

The fair value of each employee stock option and each employee stock purchase right granted is estimated on the grant date under the fair value method using the Black-Scholes valuation model. The estimated fair value of each stock option and purchase right is then expensed over the requisite service period, which is generally the vesting period. The following weighted-average assumptions were used during these periods:

	Years Ended December 31,		
	2018	2017	2016
Stock Options:			
Expected volatility	71%	68%	78%
Risk-free interest rate	3%	2%	1-2%
Expected dividend yield	0%	0%	0%
Expected life of options in years	5.7	5.8	5.7

	Years Ended December 31,		
	2018	2017	2016
Employee Stock Purchase Plan:			
Expected volatility	59%-79%	44%-62%	60%-77%
Risk-free interest rate	2.1%-2.8%	1.0%-1.7%	0.4%-1.0%
Expected dividend yield	0%	0%	0%
Expected life in years	0.5-2.0	0.5-2.0	0.5-2.0

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

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

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

Expected Life. In determining the expected life for stock options, the Company considers, among other factors, its historical exercise experience to date as well as the mean time remaining to full vesting of all outstanding options and the mean time remaining to the end of the contractual term of all outstanding options. The estimated life for the Company's employee stock purchase rights is based upon the terms of each offering period.

Stock options issued to non-employees other than directors are accounted for under the fair value method using the Black-Scholes valuation model and are re-measured to fair value at each period end until the earlier of the date that performance by the non-employee is complete or a performance commitment has been obtained.

The fair value of restricted stock units ("RSUs") is estimated based on the closing market price of the Company's common stock on the date of grant. RSUs vest annually over a four-year period.

The table below summarizes the total stock-based compensation expense included in the Company's statements of operations for the periods presented (in thousands):

	Years Ended December 31,		
	2018	2017	2016
Cost of product sales	$ 3,863	$ 3,690	$ 1,218
Research and development	32,038	26,485	18,050
Sales, general and administrative	45,663	45,357	35,997
	$ 81,564	$ 75,532	$ 55,265

Income Taxes

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

The Company recognizes the impact of a tax position in the financial statements only if that position is more likely than not of being sustained upon examination by taxing authorities, based on the technical merits of the position. Any interest and penalties related to uncertain tax positions will be reflected in income tax expense.

Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss by the weighted average number of common shares outstanding for the period, without consideration for common stock equivalents. Diluted net loss per share is computed by dividing the net loss by the weighted average number of common shares and common stock equivalents outstanding for the period determined using the treasury stock method. For purposes of this calculation, stock options, employee stock purchase rights, RSUs, and warrants are considered to be common stock equivalents but are not included in the calculations of diluted net loss per share for the periods presented as their effect would be antidilutive. The Company incurred net losses for all periods presented and there were no reconciling items for potentially dilutive securities. More specifically, at December 31, 2018, 2017 and 2016, options, employee stock purchase rights, RSUs, and warrants totaling approximately 20,824,000 shares, 18,526,000 shares and 14,739,000 shares, respectively, were excluded from the calculation of diluted net loss per share as their effect would have been anti-dilutive.

Segment Reporting

Management has determined that the Company operates in one business segment which is the development and commercialization of innovative medicines. All revenues for the years ended December 31, 2018, 2017 and 2016 were generated in the United States.

Recently Issued Accounting Standards

In December 2017, the Tax Cuts and Jobs Act (the "2017 Tax Act") was enacted. The 2017 Tax Act includes a number of changes to existing U.S. tax laws that impact the company, most notably a reduction of the U.S. corporate income tax rate from 35 percent to 21 percent for tax years beginning after December 31, 2017. The 2017 Tax Act also provides for a one-time transition tax on certain foreign earnings and the acceleration of depreciation for certain assets placed into service after September 27, 2017 as well as prospective changes beginning in 2018, including repeal of the domestic manufacturing deduction, acceleration of tax revenue recognition, global intangible low taxed income, foreign derived intangible income deduction, additional limitations on executive compensation and limitations on the deductibility of interest.

The Company recognized the income tax effects of the 2017 Tax Act in its 2017 financial statements in accordance with Staff Accounting Bulletin No. 118, which provides SEC staff guidance for the application of ASC Topic 740, *Income Taxes*, in the reporting period in which the 2017 Tax Act was signed into law. As such, the Company's financial results reflected the income tax effects of the 2017 Tax Act which the accounting under ASC Topic 740 was complete and provisional amounts for those specific income tax effects of the 2017 Tax Act which were not complete. As December 31, 2018, the impact of the 2017 Tax Act has been substantially completed. The effects of the 2017 Tax Act did not have a significant impact, and are included as part of the overall provision calculation.

In November 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 2016-18, *Statement of Cash Flows: Restricted Cash*, which requires that a statement of cash flows explain the change during the period in the total of cash, cash equivalents, and amounts generally described as restricted cash or restricted cash equivalents. Therefore, amounts generally described as restricted cash and restricted cash equivalents should be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. This guidance was effective for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. The Company adopted this guidance on January 1, 2018, using a retrospective transition method. The adoption of this ASU impacted the presentation of cash flows, with inclusion of restricted cash flows for each of the presented periods.

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments-Credit Losses: Measurement of Credit Losses on Financial Instruments*, which changes the impairment model for most financial assets and certain other instruments. For trade receivables and other instruments, entities will be required to use a new forward-looking expected loss model that generally will result in the earlier recognition of allowances for losses. For available-for-sale debt securities with unrealized losses, the losses will be recognized as allowances rather than as reductions in the amortized cost of the securities. This guidance is effective for annual reporting periods beginning after December 15, 2019, including interim periods within those years, with early adoption permitted only as of annual reporting periods beginning after December 15, 2018. The Company is currently evaluating the timing and impact of the adoption of this guidance on the Company's consolidated financial statements.

In March 2016, the FASB issued ASU 2016-09, *Compensation-Stock Compensation: Improvements to Employee Share-Based Payment Accounting*, which is intended to simplify several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, classification on the statement of cash flows, and accounting for forfeitures. This guidance was effective for annual reporting periods beginning after December 15, 2016, including interim

periods within those years. The Company adopted this guidance in the first quarter of 2017 using the modified retrospective transition method. Accordingly, the Company increased its deferred tax assets by $36.8 million, with a corresponding increase to its valuation allowance, to record previously unrecognized excess tax benefits. Additionally, the Company elected to make an accounting policy change to recognize forfeitures as they occur. As a result, the Company recorded an increase to additional paid-in capital and a corresponding increase to accumulated deficit of $0.3 million, respectively, to reflect the incremental stock-based compensation expense that would have been recognized in prior years pursuant to the modified guidance. Additionally, the Company increased its deferred tax assets by $0.1 million, with a corresponding increase to its valuation allowance, to record the excess tax benefit from the change.

In February 2016, the FASB issued ASU 2016-02, *Leases (Topic 842)*, which requires a lessee to recognize a lease liability and a right-of-use asset for all leases with lease terms of more than 12 months. This guidance is effective for annual reporting periods beginning after December 15, 2018, including interim periods within those years, and early adoption is permitted. The ASU originally required companies to adopt this guidance using a modified retrospective approach for leases that exist or are entered into after the beginning of the earliest comparative period in the financial statements. In January 2018, the FASB issued ASU 2018-01, *Leases: Land Easement Practical Expedient for Transition to Topic 842*, which facilitates the implementation of ASU 2016-02. ASU 2018-01 gives entities the option to apply ASU 2016-02 as of the effective date, rather than as of the beginning of the earliest period presented. Consequently, an entity's reporting for the comparative periods presented in the financial statements when it adopts the new leases standard will continue to be in accordance with current GAAP (ASC Topic 840) if the optional transition method is elected. The effective date of the transition requirements for the amendment is the same as the effective date and transition requirements in ASU 2016-02.

The Company adopted this standard effective January 1, 2019 using the optional transition method, and chose to apply the new standard as of the effective date. Consequently, all of the Company's operating lease commitments were recognized as lease liabilities, with corresponding right-of-use assets, based on the present value of the remaining minimum rental payments under current leasing standards for existing operating leases. Upon adoption of the standard, the Company preliminarily expects to record a right-of-use asset and lease liability of approximately $12.0 million on its Consolidated Balance Sheets. The Company has elected the standard's package of practical expedients on adoption requiring no reassessment of whether any expired or existing agreements contain a lease, the classification of any expired or existing lease agreements, or initial direct costs for any existing leases. The majority of the Company's leases are facility and equipment leases and are classified as operating leases under current lease guidance.

In May 2014, the FASB issued ASU 2014-09, *Revenue from Contracts with Customers (Topic 606)*, which supersedes nearly all existing revenue recognition guidance under GAAP. As discussed above in its Revenue Recognition Accounting Policy, the Company adopted ASU 2014-09 and all the related guidance on January 1, 2018.

3. Investments

The carrying value and amortized cost of the Company's investments, summarized by major security type, consisted of the following (in thousands):

	December 31, 2018			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Estimated Fair Value
Corporate debt securities	$ 187,371	$ 39	$ (344)	$ 187,066
Commercial paper	151,774	—	(78)	151,696
Equity Securities	3,149	—	(1,840)	1,309
	$ 342,294	$ 39	$ (2,262)	$ 340,071

	December 31, 2017			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Estimated Fair Value
U.S. Treasury notes	$ 32,976	$ —	$ (12)	$ 32,964
Government sponsored enterprise securities	10,082	—	(10)	10,072
Corporate debt securities	138,650	1	(321)	138,330
Commercial paper	90,623	—	(65)	90,558
	$ 272,331	$ 1	$ (408)	$ 271,924

The Company has classified all of its available-for-sale investment securities, including those with maturities beyond one year, as current assets on its consolidated balance sheets based on the highly liquid nature of the investment securities and because these investment securities are considered available for use in current operations. As of December 31, 2018 and December 31, 2017, the Company held $31.8 million and $48.7 million, respectively, of available-for-sale investment securities with contractual maturity dates more than one year and less than two years. The Company has classified all equity securities as other assets on its Consolidated Balance Sheets.

At December 31, 2018 the Company had 57 securities in an unrealized loss position and at December 31, 2017 the Company had 54 securities in an unrealized loss position. The following table presents gross unrealized losses and fair value for those available-for-sale investments that were in an unrealized loss position as of December 31, 2018 and December 31, 2017, aggregated by investment category and length of time that individual securities have been in a continuous loss position (in thousands):

	Less Than 12 Months		12 Months or Greater		Total	
	Estimated Fair Value	Unrealized Losses	Estimated Fair Value	Unrealized Losses	Estimated Fair Value	Unrealized Losses
December 31, 2018:						
Corporate debt securities	$ 91,265	$ (130)	$ 44,637	$ (214)	$135,902	$ (344)
Commercial paper	151,696	(78)	—	—	151,696	(78)
Total	$242,961	$ (208)	$ 44,637	$ (214)	$287,598	$ (422)
December 31, 2017:						
U.S. Treasury notes	$ 32,964	$ (12)	$ —	$ —	$ 32,964	$ (12)
Government sponsored enterprise securities	10,072	(10)	—	—	10,072	(10)
Corporate debt securities	129,820	(321)	—	—	129,820	(321)
Commercial paper	90,558	(65)	—	—	90,558	(65)
Total	$263,414	$ (408)	$ —	$ —	$263,414	$ (408)

At each reporting date, the Company performs an evaluation of impairment to determine if any unrealized losses are other-than-temporary. Factors considered in determining whether a loss is other-than-temporary include the length of time and extent to which fair value has been less than the cost basis, the financial condition of the issuer, and the Company's intent and ability to hold the investment until recovery of its amortized cost basis. The Company intends, and has the ability, to hold its investments in unrealized loss positions until their amortized cost basis has been recovered. Based on its evaluation, the Company determined that its unrealized losses were not other-than-temporary at December 31, 2018 and 2017.

4. Fair Value Measurements

The Company's investments include cash equivalents, available-for-sale investment securities consisting of money market funds, U.S. Treasury notes, and high quality, marketable debt instruments of corporations and government sponsored enterprises in accordance with the Company's investment policy, and equity investments. The Company's investment policy defines allowable investment securities and establishes guidelines relating to credit quality, diversification, and maturities of its investments to preserve principal and maintain liquidity. All investment securities have a credit rating of at least A3/A- or better, or P-1/A-1 or better, as determined by Moody's Investors Service or Standard & Poor's.

The Company's cash equivalents, available-for-sale investment securities, and equity securities are classified within the fair value hierarchy as defined by authoritative guidance. The Company's investment securities and equity securities classified as Level 1 are valued using quoted market prices. The Company obtains the fair value of its Level 2 financial instruments from third-party pricing services. The pricing services utilize industry standard valuation models whereby all significant inputs, including benchmark yields, reported trades, broker/dealer quotes, issuer spreads, bids, offers, or other market-related data, are observable. The Company validates the prices provided by the third-party pricing services by reviewing their pricing methods and matrices, and obtaining market values from other pricing sources. After completing the validation procedures, the Company did not adjust or override any fair value measurements provided by these pricing services as of December 31, 2018 and 2017, respectively.

The Company does not hold any securities classified as Level 3, which are securities valued using unobservable inputs. The Company has not transferred any investment securities between the classification levels.

The recurring fair value measurements of the Company's cash equivalents, available-for-sale investment securities, and equity securities at December 31, 2018 and 2017 consisted of the following (in thousands):

	December 31, 2018	Fair Value Measurements at Reporting Date Using		
		Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market fund	$ 34,018	$ 34,018	$ —	$ —
Equity securities	1,309	1,309	—	—
Corporate debt securities	224,474	—	224,474	—
Commercial paper	191,564	—	191,564	—
	$ 451,365	$ 35,327	$ 416,038	$ —

	December 31, 2017	Fair Value Measurements at Reporting Date Using		
		Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market fund	$ 38,057	$ 38,057	$ —	$ —
U.S. Treasury notes	32,964	32,964	—	—
Government sponsored enterprise securities	10,072	—	10,072	—
Corporate debt securities	154,396	—	154,396	—
Commercial paper	98,052	—	98,052	—
	$ 333,541	$ 71,021	$ 262,520	$ —

5. Balance Sheet Details

Inventory consisted of the following (in thousands):

	December 31,	
	2018	2017
Finished goods	$ 1,110	$ 1,164
Raw material	2,477	4,084
Work in process	483	—
	$ 4,070	$ 5,248

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

	December 31,	
	2018	2017
Machinery and equipment	$ —	$ 1,076
Computers and software	3,745	2,868
Leasehold improvements	1,655	1,642
Furniture and fixtures	2,114	1,305
Construction-in-process	—	—
	7,514	6,891
Accumulated depreciation	(4,205)	(4,229)
	$ 3,309	$ 2,662

Depreciation of property and equipment was $1.5 million, $1.2 million, and $0.8 million for the years ended December 31, 2018, 2017, and 2016, respectively. During 2018, 2017 and 2016, the Company retired $1.6 million, $0.4 million, and $0.2 million, respectively, of fully depreciated property and equipment.

Accrued liabilities consisted of the following (in thousands):

	December 31,	
	2018	2017
Accrued consulting and professional fees	$ 19,325	$ 9,395
Accrued compensation and benefits	17,028	15,260
Accrued research and development services	10,367	9,487
Accrued sales allowances	5,849	3,591
Other	3,829	2,511
	$ 56,398	$ 40,244

6. Stockholders' Equity

Public Offerings

In November 2018, the Company raised net proceeds of approximately $298.5 million from the sale of 18,602,941 shares of its common stock in a follow-on public offering, including 2,426,470 shares sold pursuant to the exercise in full of the underwriters' option to purchase additional shares.

In August 2016, the Company raised net proceeds of approximately $215.9 million from the sale of 6,969,696 shares of its common stock in a follow-on public offering, including 909,090 shares sold pursuant to the exercise in full of the underwriters' option to purchase additional shares.

In January 2016, the Company raised net proceeds of approximately $281.6 million from the sale of 10,344,827 shares of its common stock in a follow-on public offering. In connection with the January 2016 offering, the Company entered into a registration rights agreement (the "Registration Rights Agreement") with 667, L.P., Baker Brothers Life Sciences, L.P. and 14159, L.P. (the "Baker Entities"), all of which are existing stockholders of the Company and are affiliated with two of its directors, Julian C. Baker and Dr. Stephen R. Biggar. Under the Registration Rights Agreement, the Company agreed that, if the Baker Entities demand that the Company register their shares of its common stock, par value $0.0001 per share, for resale under the Securities Act of 1933, as amended (the "Securities Act"), the Company would be obligated to effect such registration. The Company's registration obligations under the Registration Rights Agreement cover all shares of its common stock now held or later acquired by the Baker Entities (including approximately $75.0 million and $43.0 million of shares that the Baker Entities purchased at the public offering price in the January 2016 and August 2016 offerings, respectively), will continue in effect for up to 10 years, and include the Company's obligation to facilitate certain underwritten public offerings of its common stock by the Baker Entities in the future. The Company has agreed to bear all expenses incurred by it in effecting any registration pursuant to the Registration Rights Agreement as well as the legal expenses of the Baker Entities of up to $50,000 per underwritten public offering effected pursuant to the Registration Rights Agreement. On April 1, 2016, pursuant to the Registration Rights Agreement, the Company filed a registration statement covering all shares owned by the Baker Entities as of March 31, 2016.

Private Equity Financings

In December 2012, the Company raised net proceeds of $80.5 million through the sale of 19,000,000 shares of its common stock at a price of $4.43 per share and the sale of warrants to purchase 500,000 shares of its common stock at a price of $4.42 per warrant share in a private equity financing. The warrants have an exercise price of $0.01 per share and will expire on December 17, 2019. In accordance with authoritative accounting guidance, the warrants' value of $2.2 million was determined on the date of grant using the Black-Scholes model with the following assumptions: risk free interest rate of 1.1 percent, volatility of 105.8 percent, a 7.0 year term and no dividend yield. These warrants were recorded as a component of stockholders' equity within additional paid-in capital. Per their terms, the warrants to purchase 500,000 shares of common stock, of which 493,145 remained outstanding at December 31, 2018, may not be exercised if the holder's ownership of the Company's common stock would exceed 19.99 percent following such exercise.

Equity Awards

The Company's 2010 Equity Incentive Plan, as amended to date (the "2010 Plan"), permits the grant of options to employees, directors and consultants. In addition, the 2010 Plan permits the grant of stock bonuses, rights to purchase restricted stock, and other stock awards. The exercise price of options granted under the 2010 Plan cannot be less than 100 percent of the fair market value of the common stock on the date of grant and the maximum term of any option is 10 years. Options granted under the 2010 Plan generally vest over a four-year period. All shares that remained eligible for grant under the Company's 2004 Equity Incentive Plan (the "2004 Plan") at the time of approval of the 2010 Plan were transferred to the 2010 Plan. The 2010 Plan share reserve also has been, and may be, increased by the number of shares that otherwise would have reverted to the 2004 Plan reserve after June 2010. In June 2015, June 2016, June 2017, and June 2018, the Company's stockholders approved amendments to its 2010 Plan to, among other things, increase the aggregate number of shares of common stock authorized for issuance under the plan by 5,000,000 shares, 3,000,000 shares, 5,500,000, and 6,700,000 shares respectively, and at December 31, 2018, there were 26,919,256 shares of common stock authorized for issuance, of which 6,676,769 shares were available for new grants under the 2010 Plan.

Stock Options

The 2004 Plan provided for the grant of options to employees, directors and consultants. The exercise price of options granted under the 2004 Plan was at 100 percent of the fair market value of the common stock on the date of grant and the maximum term of any option was 10 years. Options granted under the 2004 Plan generally vested over a four-year period.

The following table summarizes the Company's stock option activity during the year ended December 31, 2018:

	Number of Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2017	17,943,436	$ 30.42		
Granted	5,273,665	$ 19.24		
Exercised	(599,529)	$ 7.39		
Cancelled/forfeited	(2,748,791)	$ 31.19		
Outstanding at December 31, 2018	19,868,781	$ 28.04	7.6	$ 4,592
Vested and expected to vest at December 31, 2018	19,868,781	$ 28.04	7.6	$ 4,592
Exercisable at December 31, 2018	9,342,575	$ 29.50	6.4	$ 4,139

The aggregate intrinsic value of options exercisable as of December 31, 2018 is calculated as the difference between the exercise price of the underlying options and the closing market price of the Company's common stock on that date, which was $16.17 per share. The aggregate intrinsic value of options exercised during the years ended December 31, 2018, 2017, and 2016 was approximately $11.2 million, $24.4 million, and $43.2 million, respectively, determined as of the date of exercise. The Company received $4.4 million in cash from options exercised during the year ended December 31, 2018.

The weighted average per share fair value of options granted during the years ended December 31, 2018, 2017, and 2016 was approximately $12.14, $21.11, and $17.65, respectively. As of December 31, 2018, total unrecognized compensation cost related to stock options was approximately $153.7 million, and the weighted average period over which this cost is expected to be recognized is approximately 3.06 years.

Restricted Stock Units

In 2018, the Company began granting RSUs pursuant to the 2010 Plan and satisfies such grants through the issuance of new shares. RSUs are share awards that, upon vesting, will deliver to the holder shares of the Company's common stock. RSUs generally vest over a four-year period with equal vesting on anniversaries of the grant date.

The following table summarizes the Company's RSU activity during the year ended December 31, 2018:

	Number of Shares	Weighted Average Grant Date Fair Value	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2017	—	$ —	
Granted	383,811	$ 21.07	
Vested	—	$ —	
Cancelled/forfeited	(10,105)	$ 21.28	
Outstanding at December 31, 2018	373,706	$ 21.07	$ 6,042,826

As of December 31, 2018, total unrecognized compensation cost related to restricted stock options was approximately $7.5 million, and the weighted average period over which this cost is expected to be recognized is approximately 3.8 years.

Employee Stock Purchase Plan

The Company's 2004 Employee Stock Purchase Plan (the "Purchase Plan") became effective upon the closing of the Company's initial public offering in June 2004. The Purchase Plan included an "evergreen" provision providing that a limited number of additional shares may be added to the shares authorized for issuance on the date of each annual meeting of stockholders for a period of 10 years, which ended with the meeting in 2014. In June 2016, the Company's stockholders approved an amendment to the Purchase Plan to, among other things, increase the aggregate number of shares of common stock authorized for issuance under the plan by 400,000 shares, and at December 31, 2018, a total of 1,925,000 shares of common stock had been reserved for issuance under the Purchase Plan. At December 31, 2018, 154,291 shares of common stock remained available for issuance pursuant to the Purchase Plan. Eligible employees who elect to participate in an offering under the Purchase Plan may have up to 15 percent of their earnings withheld, subject to certain limitations, to purchase shares of common stock pursuant to the Purchase Plan. The price of common stock purchased under the Purchase Plan is equal to 85 percent of the lower of the fair market value of the common stock at the commencement date of each offering period or the relevant purchase date. During the years ended December 31, 2018, 2017, and 2016, a total of 233,720, 192,402, and 136,283 shares of common stock were issued under the Purchase Plan at average per share prices of $15.75, $23.50, and $22.97, respectively. The weighted average per share fair value of purchase rights granted during the years ended December 31, 2018, 2017, and 2016 was $8.25, $11.44, and $12.34, respectively. During the years ended December 31, 2018, 2017, and 2016, the Company recorded cash received from the exercise of purchase rights of $3.7 million, $4.5 million, and $3.1 million, respectively.

Settlement Agreement Proceeds

In April 2016, the Company received a payment of $14.3 million pursuant to a settlement agreement with prior 10% stockholders who sold shares of the Company's stock in 2013 that may have resulted in short-swing profits by the stockholders pursuant to Section 16(b) of the Securities Exchange Act of 1934, as amended. The Company recognized these proceeds as a capital contribution from stockholders and reflected a corresponding increase to additional paid-in capital.

7. 401(k) Plan

Effective January 1997, the Company established a deferred compensation plan (the "401(k) Plan") pursuant to Section 401(k) of the Internal Revenue Code of 1986, as amended (the "Code"), whereby substantially all employees are eligible to contribute up to 60 percent of their pretax earnings, not to exceed amounts allowed under the Code. The Company makes discretionary contributions to the 401(k) Plan equal to 100 percent of each employee's pretax contributions up to 5 percent of his or her eligible compensation, subject to limitations under the Code. The Company's total contributions to the 401(k) Plan were $3.6 million, $3.3 million, and $2.1 million for the years ended December 31, 2018, 2017, and 2016, respectively.

8. Income Taxes

Domestic and foreign pre-tax loss is as follows (in thousands):

	Years Ended December 31,		
	2018	2017	2016
Domestic	(78,112)	$ (45,249)	$ (18,419)
Foreign	(165,824)	(243,035)	(251,633)
	(243,936)	$ (288,284)	$ (270,052)

At December 31, 2018, the Company had federal, state, and foreign net operating loss ("NOL") carryforwards of approximately $393.0 million, $339.0 million, and $771.9 million, respectively. The Company recognized state income tax provisions of $1.3 million, $1.1 million and $1.3 million for the years ended December 31, 2018, 2017 and 2016, respectively. These tax liabilities were associated with California state alternative minimum tax obligations and the apportionment of income to certain state jurisdictions in which the Company did not have corresponding NOLs. Utilization of the domestic NOL and research and development ("R&D") credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations that have occurred or that could occur in the future, as required by Section 382 of the Code, as well as similar state and foreign provisions. These ownership changes may limit the amount of NOL and R&D credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an "ownership change" as defined by Section 382 of the Code results from a transaction or series of transactions over a three-year period resulting in an ownership change of more than 50 percentage points of the outstanding stock of a company by certain stockholders or public groups.

The Company previously completed a study to assess whether an ownership change, as defined by Section 382 of the Code, had occurred from the Company's formation through December 31, 2013. Based upon this study, the Company determined that several ownership changes had occurred. Accordingly, the Company reduced its deferred tax assets related to the federal NOL carryforwards and the federal R&D credit carryforwards that are anticipated to expire unused as a result of these ownership changes. These tax attributes were excluded from deferred tax assets with a corresponding reduction of the valuation allowance with no net effect on income tax expense or the effective tax rate. The Company completed a study through December 31, 2018 and concluded no additional ownership changes occurred. Future ownership changes may further limit the Company's ability to utilize its remaining tax attributes.

Federal and state NOL carryforwards of $17.0 million and less than $0.1 million will expire in 2025 and 2024, respectively, unless utilized. The remaining federal and state NOL carryforwards will begin to expire in 2026 and 2025, respectively. At December 31, 2018, the Company had $26.3 million of federal R&D credit carryforwards of which $0.1 million will expire in 2019 unless utilized, and the remaining federal R&D credit carryforwards will begin to expire in 2020. At December 31, 2018, the Company had state R&D credit carryforwards of approximately $0.5 million that will begin to expire in 2024 and $11.3 million that have no expiration date. At December 31, 2018, the Company had foreign NOL carryforwards of approximately $768.5 million that will begin to expire in 2022 and $3.4 million that have no expiration date. The Company continues to record the deferred tax assets related to these attributes, subject to valuation allowance, until expiration occurs.

Prior to the issuance of ASU 2016-09, entities were required to recognize excess tax benefit or deficiency as additional paid-in capital. To simplify the presentation of stock compensation, the amendments in this ASU require that the excess tax benefit or deficiency is recognized as expense. For public business entities, the amendments in this ASU are effective for financial statements issued for annual periods beginning after December 15, 2016 and interim periods within those annual periods. The Company adopted the update as of January 1, 2017. Given the Company's full valuation position there is no quantitative impact to the financial statements.

The components of the deferred tax assets are as follows (in thousands):

	December 31,	
	2018	2017
NOL carryforwards	$ 170,476	$ 163,059
R&D credit carryforwards	32,984	27,862
Capitalized R&D	7,421	5,606
Stock-based compensation	45,492	30,986
Other	14,750	10,110
	271,123	237,623
Valuation allowance	(271,123)	(237,623)
	$ —	$ —

Realization of deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Accordingly, the deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by approximately $33.5 million in 2018 primarily due to an increase in deferred tax assets generated from net operating losses, R&D credits and stock-based compensation expense, partially offset by the expiration of NOL carryforwards in 2018.

In December 2017, the Tax Cuts and Jobs Act (the “2017 Tax Act”) was enacted. The 2017 Tax Act included a number of changes to existing U.S. tax laws that impact the Company, most notably a reduction of the U.S. corporate income tax rate from 35 percent to 21 percent for tax years beginning after December 31, 2017. The 2017 Tax Act also provided for a one-time transition tax on certain foreign earnings, the acceleration of depreciation for certain assets placed into service after September 27, 2017 as well as prospective changes beginning in 2018, including repeal of the domestic manufacturing deduction, acceleration of tax revenue recognition, global intangible low taxed income, foreign derived intangible income deduction, additional limitations on executive compensation and limitations on the deductibility of interest.

The Company recognized the income tax effects of the 2017 Tax Act in its 2017 financial statements in accordance with Staff Accounting Bulletin No. 118, which provides SEC staff guidance for the application of ASC Topic 740, *Income Taxes*, in the reporting period in which the 2017 Tax Act was signed into law. As such, the Company’s financial results reflected the income tax effects of the 2017 Tax Act for which the accounting under ASC Topic 740 was complete and provisional amounts for those specific income tax effects of the 2017 Tax Act which were not complete. As of December 31, 2018, the accounting for the income tax effects of the 2017 Tax Act is complete. The effects of the 2017 Tax Act did not have a significant impact in 2018 and are included as part of the overall 2018 provision calculation.

A reconciliation of income taxes to the amount computed by applying the statutory federal income tax rate to the pretax loss is summarized as follows (in thousands):

	Years Ended December 31,		
	2018	2017	2016
Amounts computed at statutory federal rate	$ (51,226)	$ (98,016)	$ (91,818)
Stock-based compensation and other permanent differences	3,432	1,341	3,065
R&D credits	(7,941)	(5,573)	(3,390)
Change in valuation allowance	34,333	(28,230)	27,583
State taxes	(1,017)	(26)	272
Contingencies	2,938	360	361
Foreign rate differential	20,896	61,480	64,065
Tax Cuts and Jobs Act	—	68,889	—
Other	(159)	894	1,203
Income tax expense	$ 1,256	$ 1,119	$ 1,341

The tax years 1998-2017 remain open to examination by the major taxing jurisdictions to which the Company is subject.

The Company recognizes a tax benefit from an uncertain tax position when it is more likely than not that the position will be sustained upon examination. The Company recorded an uncertain tax position reserve of $3.1 million, $0.4 million and $0.4 million for the years ended December 31, 2018, 2017 and 2016, respectively. In addition, due to the 2017 Tax Act, an adjustment of $1.1 million was made to remeasure the uncertain tax position reserve at December 31, 2017. Due to the valuation allowance recorded against the Company's deferred tax assets, an immaterial amount of the total unrecognized tax benefits as of December 31, 2018 would reduce the annual effective tax rate if recognized. The Company does not anticipate that the amount of unrecognized tax benefits as of December 31, 2018 will significantly change within the next twelve months. The Company's practice is to recognize interest and/or penalties related to uncertain income tax positions in income tax expense. The Company had no interest and/or penalties accrued on the Company's consolidated balance sheets at December 31, 2018 or 2017, respectively. Further, the Company did not recognize any interest and/or penalties in the statement of operations for the years ended December 31, 2018, 2017 and 2016, respectively, related to uncertain tax positions.

The following table provides a reconciliation of changes in unrecognized tax benefits (in thousands):

	Years Ended December 31,		
	2018	2017	2016
Balance at beginning of period	$ 1,933	$ 2,664	$ 2,301
Additions related to current period tax positions	3,104	361	363
Provisional impact of Tax Cuts and Jobs Act	—	(1,092)	—
Balance at end of period	$ 5,037	$ 1,933	$ 2,664

9. Commitments and Contingencies

Leases and Other Long-Term Commitments

The Company leases facilities and certain equipment under noncancelable operating leases that expire at various dates through February 2031. Under the terms of the facilities leases, the Company is required to pay its proportionate share of property taxes, insurance and normal maintenance costs. Rent expense for operating leases is recorded on a straight-line basis over the life of the lease term. If an operating lease contains fixed and determinable escalation clauses, the difference between the rent expense and the rent paid is recorded as deferred rent. Rent expense under the Company's facility and equipment leases was $4.5 million, $3.8 million, and $2.8 million, for the years ended December 31, 2018, 2017, and 2016, respectively.

In 2015, the Company entered into a master lease agreement giving the Company the ability to lease vehicles under operating leases with initial terms of 36 months from the date of delivery. In 2018, the lease agreement was terminated and a new master lease agreement was entered into with a new vendor giving the Company the ability to lease vehicles under operating leases with initial terms ranging from 12 to 50 months from the date of delivery. In connection with the new lease agreement, the Company established a letter of credit for $0.4 million, which has automatic annual extensions and is fully secured by restricted cash.

In the fourth quarter of 2018, the Company entered into an agreement to lease approximately 67,020 square feet of corporate office space in San Diego, California, which is anticipated to commence in May 2020, for a term of 10 years and 9 months. The lease also provides the Company with the option to renew the lease term for two additional five year periods. In connection with this lease agreement, the Company established a letter of credit for $2.2 million, which has automatic annual extensions and is fully secured by restricted cash. No rent expense was recognized in 2018 in connection with this lease as the Company did not have access to the leased premises during the period.

The Company also enters into certain other long-term commitments for goods and services that are outstanding for periods greater than one year. To the extent these long-term commitments are noncancelable, they are reflected in the table below.

Estimated annual future minimum payments related to the Company's operating leases and other long-term contractual obligations were as follows at December 31, 2018 (in thousands):

2019	$ 4,770
2020	4,170
2021	6,906
2022	7,181
2023	6,568
Thereafter	38,683
	$ 68,278

The Company also enters into short-term agreements with various vendors and suppliers of goods and services in the normal course of operations through purchase orders or other documentation, or that are undocumented except for an invoice. Such short-term agreements are generally outstanding for periods less than a year and are settled by cash payments upon delivery of goods and services. The nature of the work being conducted under these agreements is such that, in most cases, the services may be stopped on short notice. In such event, the Company would not be liable for the full amount of the agreement and are therefore not reflected in the above table.

Royalty Payments

Pursuant to the terms of its 2006 license agreement with the Ipsen Group, the Company is required to make royalty payments of two percent of net sales of NUPLAZID.

License Agreements

In May 2018, the Company signed an Exclusivity Deed (the "Deed") with Neuren Pharmaceuticals Limited ("Neuren") that provided for exclusive negotiations for a period of three months from the date of the Deed. Under the terms of the Deed, the Company invested $3.1 million to subscribe for 1,330,000 shares of the company and paid $0.9 million for the exclusive right to negotiate a deal with Neuren, which was recorded in selling, general and administrative expenses in the Consolidated Statements of Operations for the twelve months ended December 31, 2018. At December 31, 2018, the Company continues to hold the equity securities as a strategic investment in which the Company does not have a controlling interest or significant influence. Publicly held equity securities are measured using quoted prices in their respective active markets with changes recorded through other expense on the statements of operations. Net loss on strategic investments recognized in other expense in the Consolidated Statements of Operations for the twelve months ended December 31, 2018 was $1.8 million. As of December 31, 2018, the aggregate carrying amount of the Company's strategic equity investment was $1.3 million included in other assets on the Consolidated Balance Sheets.

In August 2018, the Company entered into a license agreement with Neuren and obtained exclusive North American rights to develop and commercialize trofinetide for Rett syndrome and other indications. Under the terms of the agreement, Neuren received an upfront payment of $10.0 million and is eligible to receive milestone payments of up to $455.0 million, based on the achievement of certain development and annual net sales milestones. In addition, Neuren is eligible to receive tiered, escalating, double-digit percentage royalties based on net sales. The license agreement was accounted for as an asset acquisition and the upfront cash payment of $10.0 million has been recorded in research and development expenses in the Consolidated Statements of Operations for the twelve months ended December 31, 2018, as there is no alternative use for the asset.

Corporate Credit Card Program

In connection with the Company's credit card program, the Company established a letter of credit in 2016 for $2.0 million, which has automatic annual extensions and is fully secured by restricted cash.

Legal Proceedings

Between July 19 and August 3, 2018, following recent negative publicity about NUPLAZID, three purported Company stockholders filed putative securities class action complaints (captioned Staublein v. ACADIA Pharmaceuticals, Inc., Case No. 18-cv-01647, Stone v. ACADIA Pharmaceuticals Inc., Case No. 18-cv-01672, and Barglow v. ACADIA Pharmaceuticals Inc., Case No. 18-cv-01812) in the U.S. District Court for the Southern District of California against the Company and certain of its current and former 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 the Company's 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 the Company engaged in business practices likely to attract regulatory scrutiny. The complaints seek unspecified monetary damages and other relief. Several putative lead plaintiffs filed motions to consolidate the cases and to appoint a lead plaintiff. On January 3, 2019, the court consolidated the cases under Case No. 18-cv-01647 and took the lead plaintiff motions under submission. The defendants' response to the complaints is stayed pending resolution of the lead plaintiff motions. The Company has assessed such legal proceedings, and given the unpredictability inherent in litigation, the Company cannot predict the outcome of these matters. At this time, the Company is unable to estimate possible losses or ranges of losses that may result from such legal proceedings, and it has not accrued any amounts in connection with such legal proceedings other than ongoing attorneys' fees.

Government Investigation

In September 2018 the Company received a civil investigative demand ("CID") from the Department of Justice ("DOJ") requesting certain documents and information related to the Company's sales and marketing of NUPLAZID. The Company is 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.

10. Selected Quarterly Financial Data (Unaudited)

The following financial information reflects all normal recurring adjustments, which are, in the opinion of management, necessary for a fair statement of the results of the interim periods. Summarized quarterly data for the years ended December 31, 2018 and 2017 are as follows (in thousands, except per share data):

	Fiscal Year 2018 Quarters				
	1st	2nd	3rd	4th	Total
Revenues	$ 48,868	$ 57,063	$ 58,305	$ 59,571	$ 223,807
Gross profit[1]	$ 46,715	$ 53,501	$ 54,466	$ 56,748	$ 211,430
Net loss	$ (54,296)	$ (63,266)	$ (62,138)	$ (65,492)	$ (245,192)
Basic and diluted net loss per share[2]	$ (0.44)	$ (0.51)	$ (0.50)	$ (0.50)	$ (1.94)

	Fiscal Year 2017 Quarters				
	1st	2nd	3rd	4th	Total
Revenues	$ 15,286	$ 30,475	$ 35,578	$ 43,562	$ 124,901
Gross profit[1]	$ 13,023	$ 28,251	$ 33,443	$ 41,107	$ 115,824
Net loss	$ (87,843)	$ (67,441)	$ (65,248)	$ (68,871)	$ (289,403)
Basic and diluted net loss per share[2]	$ (0.72)	$ (0.55)	$ (0.53)	$ (0.55)	$ (2.36)

(1) Determined by subtracting cost of product sales from product sales, net.

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

SCHEDULE II – Valuation and Qualifying Accounts
(in thousands)

	Balance at Beginning of Period	Additions: Provision Related to Current Period Sales	Deductions: Actual Distribution Fees, Discounts and Chargebacks Related to Current Period Sales	Deductions: Actual Distribution Fees, Discounts and Chargebacks Related to Prior Period Sales	Balance at End of Period
Allowance for distribution fees, discounts and chargebacks:					
For the year ended December 31, 2016	$ —	$ 2,163	$ (1,962)	$ —	$ 201
For the year ended December 31, 2017	$ 201	$ 12,837	$ (12,591)	$ (201)	$ 246
For the year ended December 31, 2018	$ 246	$ 24,613	$ (22,773)	$ (246)	$ 1,840

MANAGEMENT TEAM

Stephen R. Davis
Chief Executive Officer

Srdjan (Serge) Stankovic, M.D., M.S.P.H.
President

Austin Kim
Executive Vice President,
General Counsel and Secretary

Elena Ridloff, CFA
Executive Vice President,
Chief Financial Officer

Michael J. Yang
Executive Vice President,
Chief Commercial Officer

Daryl DeKarske
Senior Vice President,
Global Head of Regulatory Affairs

Robert Kaper, M.D.
Senior Vice President,
Global Head of Medical Affairs

Charmaine Lykins
Senior Vice President,
Marketing

Bob Mischler
Senior Vice President,
Strategy and Technology Operations

Amanda Morgan
Senior Vice President,
Sales and Market Access

Randall Owen, M.D.
Senior Vice President,
Clinical Development and Chief Medical Officer

Eliseo Salinas, M.D., M.Sc.
Senior Vice President,
Chief Scientific Officer and Head of External Innovation

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Baker Bros. Advisors LP

Laura A. Brege
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Cervantes Life Science Partners

Jim Daly
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Incyte Corporation

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Edmund P. Harrigan, M.D.
Former Senior Vice President,
Worldwide Safety and Regulatory
Pfizer Inc.

Daniel B. Soland
Former Chief Executive Officer
uniQure N.V.

CORPORATE HEADQUARTERS

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COMMON STOCK LISTING

Ticker Symbol: ACAD,
The NASDAQ Global Select Market

ANNUAL STOCKHOLDERS' MEETING

ACADIA Pharmaceuticals' Annual Stockholders' Meeting
will be held on Wednesday, June 26 2019, at the
Hilton La Jolla Torrey Pines, 10950 North Torrey Pines Road,
La Jolla, CA 92037

STOCK TRANSFER AGENT AND REGISTRAR

Computershare Trust Company, N.A.
462 South 4th Street Suite 1600
Louisville, KY 40202
Telephone: (800) 851-3061
www.computershare.com/us

INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

Ernst & Young LLP

STOCKHOLDERS' INQUIRIES

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

FORWARD-LOOKING STATEMENTS

Statements in this report that are not strictly historical in nature are forward-looking statements. These statements include but are not limited to statements related to the potential opportunity for future growth in sales of NUPLAZID, including through sales of new dosages and forms; the timing of ongoing and future clinical studies for pimavanserin; the development and commercialization of trofinetide; and guidance for full-year 2019 NUPLAZID net sales and certain expense line items. These statements are only predictions based on current information and expectations and involve a number of risks and uncertainties. Actual events or results may differ materially from those projected in any of such statements due to various factors, including the risks and uncertainties inherent in drug development, approval and commercialization, and the fact that past results of clinical trials may not be indicative of future trial results. For a discussion of these and other factors, please refer to ACADIA's annual report on Form 10-K for the year ended December 31, 2018 as well as ACADIA's subsequent filings with the Securities and Exchange Commission. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. All forward-looking statements are qualified in their entirety by this cautionary statement and ACADIA undertakes no obligation to revise or update this report to reflect events or circumstances after the date hereof, except as required by law.

ACADIA Pharmaceuticals Inc.
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