SUPERNUS PHARMACEUTICALS INC
Form 10-K
March 01, 2019

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

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

FOR THE FISCAL YEAR ENDED DECEMBER 31, 2018

COMMISSION FILE NUMBER: 001-35518

or

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

FOR THE TRANSITION PERIOD FROM TO

SUPERNUS PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware		**20-2590184**
(State or other jurisdiction of incorporation or organization)		(I.R.S. Employer Identification Number)
1550 East Gude Drive, Rockville, MD	**(301) 838-2500**	**20850**
(Address of Principal Executive Offices)	(Registrant's telephone number, including area code)	(zip code)

SECURITIES REGISTERED PURSUANT TO SECTION 12(b) OF THE ACT:

TITLE OF EACH CLASS:	**NAME OF EACH EXCHANGE ON WHICH REGISTERED:**
Common Stock, $0.001 Par Value	The NASDAQ Stock Market LLC

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 ý No o

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes o No ý

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 ý No o

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 (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ý No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of 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. o

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

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

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. o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes o No ý

As of June 30, 2018, the aggregate market value of the common stock held by non-affiliates of the registrant based on the closing price of the common stock on The NASDAQ Global Market was $3,020,270,520.

The number of shares of the registrant's common stock outstanding as of February 13, 2019 was 52,320,473.

DOCUMENTS INCORPORATED BY REFERENCE

Certain portions of the registrant's definitive Proxy Statement for its 2019 Annual Meeting of Stockholders, which will be filed with the Securities and Exchange Commission not later than 120 days after the end of the registrant's 2018 fiscal year end, are incorporated by reference into Part III of this Annual Report on Form 10-K.

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SUPERNUS PHARMACEUTICALS, INC.
FORM 10-K

For the Year Ended December 31, 2018

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Unless the content requires otherwise, the words "Supernus," "we," "our" and "the Company" refer to Supernus Pharmaceuticals, Inc. and its subsidiary.

We are the owners of various U.S. federal trademark registrations(®) and registration applications( ), including the following marks referred to in this Annual Report on Form 10-K pursuant to applicable U.S. intellectual property laws: "Supernus®," "Oxtellar XR®," "Trokendi XR®," "Microtrol®," "Solutrol®," and the registered Supernus Pharmaceuticals logo.

All other trademarks or trade names referred to in this Annual Report are the property of their respective owners. Solely for convenience, the trademarks and trade names in this Annual Report on Form 10-K are referred to without the ® and *TM* symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

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PART I

This Annual Report on Form 10-K contains forward-looking statements, within the meaning of the Securities Exchange Act of 1934 and the Securities Act of 1933, that involve risks and uncertainties. Forward-looking statements convey our current expectations or forecasts of future events. All statements contained in this Annual Report other than statements of historical fact are forward-looking statements. Forward-looking statements include statements regarding our future financial position, business strategy, budgets, projected costs, plans and objectives of management for future operations. The words "may," "continue," "estimate," "intend," "plan," "will," "believe," "project," "expect," "seek," "anticipate," "should," "could," "would," "potential," or the negative of those terms and similar expressions may identify forward-looking statements, but the absence of these words does not necessarily mean that a statement is not forward-looking. You should not place undue reliance on these forward-looking statements, which speak only as of the date of this report. All of these forward-looking statements are based on information available to us at this time, and we assume no obligation to update any of these statements. Actual results could differ from those projected in these forward-looking statements as a result of many factors, including those identified in the "Business," "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections and elsewhere in this Annual Report on Form 10-K. We urge you to review and consider the various disclosures made by us in this report, and those detailed from time to time in our filings with the Securities and Exchange Commission, that attempt to advise you of the risks and factors that may affect our future results.

ITEM 1. BUSINESS.

Overview

Supernus Pharmaceuticals, Inc. (the Company) was incorporated in Delaware and commenced operations in 2005. The Company became publicly traded in 2012 and is listed on The Nasdaq Stock Exchange under the ticker symbol SUPN. Our principal executive offices are in Rockville, Maryland.

We are a pharmaceutical company focused on developing and commercializing products for the treatment of central nervous system (CNS) diseases. Our extensive expertise in product development has been built over the past 25 years: initially as a privately-held stand-alone development organization, then as a United States (U.S.) subsidiary of Shire Plc and, upon our acquisition of substantially all of the assets of Shire Laboratories Inc. in late 2005, as Supernus Pharmaceuticals.

On October 4, 2018, we acquired Biscayne Neurotherapeutics, Inc. (Biscayne), a privately-held company developing a novel treatment for epilepsy. We obtained worldwide rights, excluding certain markets in Asia where rights have been out-licensed, to Biscayne's product candidate, SPN-817 (huperzine A). SPN-817 is in clinical development and has received an Orphan Drug designation for Dravet Syndrome from the U.S. Food and Drug Administration (FDA).

We market two products, Oxtellar XR and Trokendi XR in the U.S. Oxtellar XR and Trokendi XR are the first once-daily extended release oxcarbazepine and topiramate products indicated for the treatment of epilepsy in the U.S. market. In April 2017, we launched Trokendi XR for the prophylaxis of migraine headache in adults and adolescents. In December 2018, the FDA approved the Company's supplemental new drug application (sNDA) for Oxtellar XR to include monotherapy treatment of partial onset seizures of epilepsy in adults and in children 6 to 17 years of age. We market our products through our own sales force and seek strategic collaborations with other pharmaceutical companies to license and commercialize our products outside the United States.

Our net product revenues of $399.9 million in 2018 were driven by strong growth in prescriptions for Oxtellar XR and Trokendi XR. Total prescriptions as reported by IQVIA (formerly Intercontinental Marketing Services (IMS)) have shown a steady year over year increase as shown in the following graph.

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Source: IQVIA Monthly Prescriptions (as restated by IQVIA for 2017 and 2018)

As of year-end 2018, Trokendi XR represented approximately 5% of the large base of prescriptions for topiramate, and Oxtellar XR represented approximately 3% of the oxcarbazepine market. Total annual prescriptions for the topiramate market and the oxcarbazepine market are approximately 14.6 million and 4.8 million, respectively. We expect to continue to grow our revenues for Oxtellar XR and Trokendi XR by continuing to drive penetration in these markets. We believe these products with their current indications in the neurology market, which include the recently approved monotherapy indication for Oxtellar XR, have the potential to achieve combined annual peak net sales in excess of $500 million.

We are developing multiple proprietary product candidates in the CNS market to address significant unmet medical needs and market opportunities. We are developing SPN-812 (viloxazine hydrochloride) as a novel, non-stimulant candidate to treat patients who have attention deficit hyperactivity disorder (ADHD). In December 2018, we reported favorable results from three of the four pivotal Phase III trials for SPN-812 with data from the fourth trial expected late first quarter 2019. We anticipate filing a new drug application (NDA) with the FDA in the second half of 2019, and to launch SPN-812, pending U.S. Food and Drug Administration approval, in the second half of 2020.

In addition, we are initially developing SPN-810 (molindone hydrochloride) to treat impulsive aggression (IA) in children and adolescents who have ADHD. We plan to subsequently develop SPN-810 for the treatment of IA in other CNS diseases, such as autism, post traumatic stress disorder (PTSD), bipolar disorder, schizophrenia, Alzheimer's and other forms of dementia. There are currently no approved products in the U.S. indicated for the treatment of IA.

Furthermore, we are developing SPN-604 (extended release oxcarbazepine) for the treatment of bipolar disorder, which would be a new indication for oxcarbazepine. Following our acquisition of Biscayne, we are currently developing SPN-817 in severe pediatric epilepsy disorders.

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Products and Product Candidates

The table below summarizes our current portfolio of novel products and product candidates.

Product	Indication	Status
Oxtellar XR	Epilepsy	In the market
Trokendi XR	Epilepsy	In the market
	Migraine*	In the market
SPN-812	ADHD	Phase III
SPN-810	IA**	Phase III
SPN-604	Bipolar	Phase III***
SPN-809	Depression	Phase II ready
SPN-817	Epilepsy	Phase I

*
Prophylaxis of migraine headache in adults and adolescents.

**
Initial program is for IA in patients with ADHD, with plans to add other indications, such as IA in patients with autism, PTSD, bipolar disorder, Alzheimer's and other forms of dementia.

***
Phase III clinical program to start in second half of 2019

We have a successful track record of developing and launching novel products by applying proprietary technologies to known drugs to improve their side effect profile or to improve patient compliance. In addition, we have developed new indications for existing therapies. Our key proprietary technology platforms include: Microtrol, Solutrol and EnSoTrol. These technologies have been utilized to create ten marketed products, including Trokendi XR and Oxtellar XR, Adderall XR (developed for Shire), Intuniv (developed for Shire), Mydayis (developed for Shire), and Orenitram (developed for United Therapeutics Corporation), as well as our key product candidates SPN-812 and SPN-810.

We continue to build our intellectual property portfolio to provide protection for our technologies, products and product candidates.

Our Strategy

Our vision is to be a leading pharmaceutical company developing and commercializing new medicines for treatment of CNS diseases in neurology and psychiatry. Key elements of our strategy to achieve this vision are to:

Drive growth and profitability. We will continue to drive the prescription growth of Trokendi XR and Oxtellar XR by continuing to dedicate sales and marketing resources in the U.S.

Advance our pipeline toward commercialization. We are continuing with the Phase III clinical trials for SPN-812, a novel non-stimulant treatment for ADHD, and with the Phase III clinical trials for SPN-810, a novel treatment for IA in patients who have ADHD. We expect to file an NDA with the FDA for the approval of SPN-812 in second half of 2019.

Target strategic business development opportunities. We are actively exploring a broad range of strategic opportunities that fit well with our strong presence in CNS while also exploring other disease areas that are driven by specialty physicians such as orphan or rare diseases. These strategic options include: in-licensing products and/or entering into development collaborations leading to commercialization rights; opportunities that leverage and/or expand our sales force call points for our marketed products and product candidates; co-development partnerships outside the U.S. for our pipeline products; and growth opportunities through value-creating and

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transformative merger and acquisition transactions, including both commercial stage and development stage products.

Continue to grow our pipeline. We plan to continue to evaluate and develop additional CNS product candidates that we believe have significant commercial potential through our internal research and development efforts.

Our Neurology Portfolio

Our neurology portfolio consists of Oxtellar XR, which is the first and only once-daily extended release oxcarbazepine product indicated for patients with epilepsy, and Trokendi XR, which is the first once-daily extended release topiramate product indicated for patients with epilepsy. We launched Trokendi XR for the prophylaxis of migraine headache in the U.S. market in April 2017. These products differ from immediate release formulations by offering once-daily dosing and unique pharmacokinetic profiles, which we believe can have very positive clinical effects for many patients. We believe a once-daily dosing regimen improves adherence, making it more probable that patients maintain sufficient levels of medication in their bloodstreams to protect against seizures and migraines. In addition, we believe that the unique smooth and steady pharmacokinetic profiles of our once-daily formulations reduce the peak to trough blood level fluctuations, which are typically associated with immediate release products and which may result in increased adverse events (AEs), more side effects and decreased efficacy.

Epilepsy Overview

Epilepsy is a complex neurological disorder characterized by spontaneous recurrence of unprovoked seizures, which are sudden surges of electrical activity in the brain that impair a person's mental and/or physical abilities.

Compliance with drug treatment regimens is critically important to achieving effective control for patients with epilepsy. Non-compliance with anti-epileptic drug (AED) therapy is a serious issue and remains the most common cause of breakthrough seizures for patients. Not only is taking all prescribed doses critical to control breakthrough seizures, but the timing of when patients take their prescribed doses can also be crucial.

We believe extended release products, and in particular Trokendi XR and Oxtellar XR, may offer important advantages in the treatment of epilepsy. The release profiles of extended release products can produce more consistent and steadier plasma concentrations as compared to immediate release products, potentially resulting in fewer side effects, better tolerability, fewer emergency room visits, improved efficacy, and fewer breakthrough seizures. Improved tolerability may help patients improve adherence and correspondingly, help patients enjoy a better quality of life.

In addition, when considering treatment regimens for patients with epilepsy, neurologists and epileptologists, take into consideration the mechanism of action (MOA) of the different anti-epileptics that are available. By combining several different MOAs, it is sometimes possible to get significantly better seizure control. We recently acquired SPN-817, an antiepileptic, which we believe has a MOA that is different from what is currently available and can represent a unique additional treatment alternative for physicians and patients.

Migraine Overview

Approximately 39 million individuals in the U.S. are affected by migraine. The World Health Organization categorizes migraine as one of the most disabling medical illnesses worldwide.

Migraine is a painful complex neurological disorder, consisting of recurring, painful attacks that can significantly disrupt time with loved ones, education and careers. Migraine headaches are often

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characterized by throbbing pain, extreme sensitivity to light or sound and, potentially, nausea and vomiting.

As in epilepsy, we believe extended release products, and in particular Trokendi XR, may offer important advantages for treatment of migraine. The release profiles of extended release products can produce more consistent and steadier plasma concentrations as compared to immediate release products, potentially resulting in fewer side effects, better tolerability, fewer emergency room visits and improved efficacy. Improved tolerability may help patients improve adherence, have fewer breakthrough migraines and, correspondingly, help patients enjoy a better quality of life.

Commercial Products

Trokendi XR

Trokendi XR is a once-daily extended release topiramate product indicated for patients with epilepsy and for prevention of migraine headache in the U.S. market, and is designed to improve patient adherence over the current immediate release products which must be taken multiple times per day. Trokendi XR is indicated for initial monotherapy in patients 6 years of age and older with partial onset or primary generalized tonic-clonic (PGTC) seizures, as add-on therapy in patients 6 years of age and older with partial onset or PGTC seizures or with seizures associated with Lennox-Gastaut syndrome, and for prophylaxis of migraine headaches in adults and adolescents 12 years of age and older. Trokendi XR's pharmacokinetic profile results in lower peak plasma concentrations, higher trough plasma concentrations, and slower plasma uptake rates. This results in smoother and more consistent plasma concentrations than immediate release topiramate formulations. We believe that such a profile mitigates blood level fluctuations that are frequently associated with many side effects and reduces the likelihood of breakthrough seizures and migraine headaches that patients can suffer when taking immediate release products. Side effects associated with immediate release products may lead patients to skip doses, which could place them at higher risk for breakthrough seizures and migraine headaches.

Oxtellar XR

Oxtellar XR is the only once-daily extended release oxcarbazepine product indicated in the U.S. for treatment of patients with epilepsy. Oxtellar XR is indicated as therapy of partial onset seizures in adults and in children 6 years to 17 years of age. With its novel pharmacokinetic profile showing lower peak plasma concentrations, a slower rate of plasma input, and smoother and more consistent blood levels compared to immediate release products, we believe Oxtellar XR improves the tolerability of oxcarbazepine and thereby reduces side effects. In addition, Oxtellar XR once-per-day dosing is designed to improve patient adherence compared to the current immediate release products that must be taken multiple times per day.

Product Candidates

SPN-817 (huperzine A)

SPN-817 will utilize a novel synthetic form of huperzine A, whose MOA includes potent acetyl cholinesterase inhibition with pharmacological activities in CNS conditions such as epilepsy. SPN-817 will have new chemical entity status (NCE) in the U.S. market. We expect to have significant intellectual property (IP) protecting this product candidate through our own research and development efforts as well as through in-licensed IP. SPN-817 represents a novel MOA for an anticonvulsant. Development will initially focus on the drug's anticonvulsant activity that has been shown in preclinical models for partial seizures and Dravet Syndrome.

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SPN-817 Development Program

We plan on studying SPN-817 initially in severe pediatric epilepsy disorders. A Phase I proof-of-concept trial is currently underway in adult patients with refractory complex partial seizures to study the safety and pharmacokinetic profile of a new extended release formulation of non-synthetic huperzine A.

We will focus on completing and optimizing the synthesis process of the drug and the development of a novel dosage form. Given the potency of huperzine A, a novel extended release oral dosage form is critical to the success of this program because initial studies with immediate release formulations of non-synthetic huperzine A have shown dose-limiting serious side effects.

Manufacturing

We currently depend on third-party commercial manufacturing organizations (CMOs) for all manufacturing operations, including production of raw materials, dosage form product and product packaging. This encompasses product for commercial use, as well as product for preclinical research and clinical trials.

We have entered into agreements with leading CMOs headquartered in North America, including Patheon Pharmaceuticals, Inc., Packaging Coordinators, Inc. and Catalent Pharma Solutions, for the manufacture and packaging of the final commercial products Oxtellar XR and Trokendi XR. These CMOs offer a comprehensive range of contract manufacturing and packaging services. Commercial products as well as our product candidates are sourced from single third-party suppliers.

We do not own or operate manufacturing facilities for the production of any of our product candidates beyond Phase II clinical trials, nor do we have plans to develop our own manufacturing operations for Phase III clinical materials or commercial products in the foreseeable future. We currently employ internal resources to manage our manufacturing contractors.

Sales and Marketing

We have a commercial organization in the U.S. to support current and future sales of Oxtellar XR and Trokendi XR. We believe our current sales force of over 200 sales representatives is effectively targeting healthcare providers, primarily neurologists, to support and grow our epilepsy and migraine franchise. Simultaneously promoting two neurology products allows us to leverage our commercial infrastructure.

Assuming we obtain FDA approval for the product candidates currently in our pipeline, we anticipate adding sales representatives to market our products to the relevant population of physicians, primarily psychiatrists.

Epilepsy Competition

Trokendi XR competes with all immediate release and extended release topiramate products, including Topamax, Qudexy XR and their related generic products. Oxtellar XR competes with all immediate release oxcarbazepine products, including Trileptal and its related generic products. Both Oxtellar XR and Trokendi XR compete with other anti-epileptic products, both branded and generic.

Migraine Competition

Trokendi XR competes with all immediate release and extended release topiramate products, including Topamax, Qudexy XR and their related generic products, as well as other products used for the prevention of migraine headaches, such as anti-CGRP (calcitonin gene related peptide), Botox, beta-blockers, valproic acid and amitriptyline.

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Our Psychiatry Portfolio

Our psychiatry portfolio includes four product candidates for the treatment of psychiatric disorders:

SPN-812, the most advanced product candidate, is being developed for ADHD. Positive topline data from three successful Phase III clinical trials were reported in 2018, and data from a fourth Phase III trial is expected to be released in late first quarter of 2019.

SPN-810 has fast track status and is expected to be the first product approved for treatment of IA. Phase III clinical trials are expected to be completed in 2019 in patients 6 years to 11 years old while a trial in adolescents continues into 2020.

SPN-809 employs the same active ingredient in SPN-812 and is being developed for depression. SPN-809 is Phase II ready.

SPN-604 is being developed for the treatment of bipolar. Phase III clinical trials are planned to be initiated in the second half of 2019.

ADHD Overview

ADHD is a common CNS disorder characterized by developmentally inappropriate levels of inattention, hyperactivity and impulsivity. ADHD affects an estimated 6% to 9% of all school-age children and 3% to 5% of adults in the United States[(1)]. An estimated 50% of children with ADHD continue to meet criteria for ADHD into adolescence[(2)]. Current non-stimulant treatments for ADHD account for about 8% of the total ADHD prescriptions in the U.S. during 2018. The ADHD market is projected to grow at 2% annually, from approximately 74 million prescriptions in 2018 to approximately 78 million prescriptions by 2020. For the year ended December 31, 2018, according to data from IQVIA, the U.S. market for ADHD prescription drugs was $9.1 billion.

Diagnosis of ADHD requires a comprehensive clinical evaluation based on identifying patients who exhibit the core symptoms of inattention, hyperactivity, and impulsivity. Although many children may be inattentive, hyperactive or impulsive, the level of severity and degree of functional impairment, as well as considerations of what may be behind the underlying symptoms, determine which children meet the diagnosis and should be treated for ADHD.

IA Overview

The ADHD market represented roughly 74 million prescriptions in 2018, growing approximately 2% over 2017. By 2020, we project that the ADHD market will reach approximately 78 million prescriptions. Of these 78 million prescriptions, roughly one-third will be written for patients with IA or with IA and other comorbidities.

IA is not limited to individuals with ADHD. We believe, based on our market research, that IA occurs in patients with other CNS disorders, including autism, Alzheimer's and other forms of dementia, bipolar disorder, PTSD, oppositional defiant disorder, conduct disorder and intermittent explosive disorder. Market research we have conducted indicates that the prevalence of IA in autistic children and adolescents is approximately 45%, and the prevalence of IA in children and adolescents with bipolar disorder is approximately 60%.

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(1) Dopheide, J.A., *Attention-Deficit- Hyperactivity Disorder: An Update*, published June 2009 in *Pharmacotherapy*.

(2) Floet, A.M.W., *Attention- Deficit/Hyperactivity Disorder*, published February 2010 in *Pediatrics in Review*.

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Current Treatments for IA in Patients with ADHD

Currently, there are no approved medications in the U.S. for the treatment of IA. IA is present in individuals who spontaneously react more aggressively and strongly than normal to stimuli by committing verbal or physical acts against people, property or themselves. Based on our discussions with medical experts, the current treatment options for IA in patients with ADHD include psychosocial interventions, such as school-based or family-based behavioral therapies, which are often not wholly effective. In the large, multisite Multimodal Treatment Study of Children with ADHD[(3)], a seminal clinical trial designed by experts from key stakeholder communities such as the National Institute of Mental Health, researchers observed that after 14 months of either ADHD medication-only or a regimen that combined ADHD medication with behavioral interventions, 44% of those children with ADHD (or 26% of the total sample size in the trial) who initially exhibited aggression still had what can be described as IA at the end of the trial. This demonstrates that psychosocial interventions may not work for a large percentage of children with ADHD who exhibit aggressive behaviors.

In response, doctors have also tried to treat patients with IA by off-label use of prescription medicines, such as mood stabilizers, stimulants and anti-psychotic drugs. Results have varied, but anti-psychotic drugs appear to have the best therapeutic potential. Unfortunately, many of these agents are associated with adverse effects, including obesity, dyskinesia, lipid abnormalities, marked increases in prolactin and increase in diabetes, which is of particular concern when treating pediatric populations. None of these agents are approved for treatment of IA.

Product Candidates

SPN-812 (viloxazine hydrochloride)

We are developing SPN-812 as a novel non-stimulant treatment for ADHD with the potential to address a $9.1 billion market opportunity in the U.S. for the treatment of ADHD. SPN-812, a norepinephrine reuptake inhibitor with selective serotonin modulation activity, would provide an additional option to the few non-stimulant therapies currently available. We believe that SPN-812 could be more effective than other non-stimulant therapies due to its unique pharmacological profile, and offers physicians an alternative to stimulant therapy.

We expect to submit an NDA for SPN-812 in the second half of 2019, and to launch it, pending FDA approval, in the second half of 2020. We expect SPN-812, if approved, to have five year market exclusivity given its NCE status in the U.S. Further, we are developing IP covering the novel synthesis process for the active ingredient in SPN-812, its novel use in ADHD and its novel extended release delivery.

SPN-812 Development Program

We initiated four Phase III clinical trials for SPN-812 in September 2017, three of which are clinically complete. The program consists of four three-arm, placebo-controlled trials: P301 and P303 trials in patients 6 years to 11 years old and P302 and P304 trials in patients 12-17 years old. We announced positive topline results from the pediatric trials (P301 and P303) and the first adolescent trial (P302) in December 2018. Results of the second adolescent Phase III trial (P304) are expected by the end of the first quarter of 2019. Refer to the Company's Annual Report on Form 10-K for the year ended December 31, 2017 for the results of the Phase IIb trials.

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(3) The MTA Cooperative Group, *A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder*, published December 1999 in *Archives of General Psychiatry*.

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Results of P301 and P303 Phase III trials

Both studies were randomized, double-blind, placebo controlled, multicenter, parallel group clinical trials in children 6 years to 11 years of age diagnosed with ADHD. Each treatment was administered orally once a day over five weeks in study P301 and seven weeks in study P302, after the titration phase.

A total of 477 patients were randomized in the P301 study across placebo and two doses of SPN-812 (100mg/200mg). A total of 313 patients were randomized in the P303 study across placebo and two doses of SPN-812 (200mg/400mg). The primary objective of both studies was to assess the effect of SPN-812 in reducing the symptoms of ADHD in children. The primary outcome measure was the change from baseline to the end of the study in the ADHD Rating Scale (RS)-5 total score. Safety and tolerability of SPN-812 were assessed by the monitoring of AEs, clinical laboratory tests, vital signs, ECGs, suicidality and physical examinations. Patients who completed the study were offered the opportunity to continue into an open-label phase that is currently on-going.

On December 6, 2018, we announced positive topline results from our Phase III studies of SPN-812 in children for the treatment of ADHD. The trials were successful in meeting the primary endpoint, demonstrating that SPN-812 at daily doses of 100mg and 200mg in study P301 and 200mg and 400mg in study P303 achieved a statistically significant improvement in the symptoms of ADHD from baseline to end of study as measured by the ADHD-RS-5. All SPN-812 doses tested in the trials were well tolerated.

At the end of the P301 Study, SPN-812 100 mg and 200 mg doses reached statistical significance compared to placebo in the primary endpoint. Patients receiving SPN-812 100 mg and 200 mg had a 16.6 point change ($p=0.0004$) and a 17.7 point change ($p<0.0001$) from baseline, respectively, in the primary endpoint vs. 10.9 for placebo at week 6. This primary result, based on Mixed Model Repeated Measures (MMRM) analysis in the Intent-To-Treat (ITT) population, was confirmed by sensitivity analyses using Analysis of Covariance (ANCOVA) (100 mg, $p=0.0008$; 200 mg, $p<0.0001$).

The study demonstrated fast onset of action, reaching statistical significance for 100 mg and 200 mg doses as early as week 1 with p- values of 0.0004 and 0.0244, respectively. Statistical significance was maintained on a weekly basis through the end of the trial at week 6. In addition, at the end of the study, SPN-812 100 mg and 200 mg reached statistical significance compared to placebo on the hyperactivity/impulsivity and inattention subscales of the ADHD-RS-5 scale with p- values ranging from <0.0001 to 0.0026. Finally, SPN-812 100 mg and 200 mg met all secondary endpoints, including the important analysis of the Clinical Global Impression Improvement (CGI-I) secondary endpoint, with p- values of 0.002 and <0.0001, respectively, compared to placebo.

At the end of the P303 Study, SPN-812 200 mg and 400 mg doses reached statistical significance compared to placebo in the primary endpoint. Patients receiving SPN-812 200 mg and 400 mg had a 17.6 point change ($p=0.0038$) and a 17.5 point change ($p=0.0063$) from baseline, respectively, in the primary endpoint vs. 11.7 for placebo at week 8. This primary result, based on MMRM analysis in the ITT population, was confirmed by sensitivity analyses using ANCOVA (200 mg, $p=0.0058$; 400 mg, $p<0.0121$). Onset of action for SPN-812 showed clear differences compared to placebo starting by week 1, reaching statistical significance at week 5, which was sustained through the rest of the trial. Similar to the P301 study, at the end of the P303 study, SPN-812 200 mg and 400 mg reached statistical significance compared to placebo on the hyperactivity/impulsivity and inattention subscales of the ADHD-RS-5 scale with p- values ranging from 0.0020 to 0.0248. In addition, SPN-812 200 mg and 400 mg met the CGI-I secondary endpoint with p- values of 0.0028 and 0.0099, respectively, compared to placebo.

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Overall, both trials exhibited favorable tolerability and safety profiles with low incidence of AEs across all doses. AEs were mild leading to low discontinuation rates due to AEs of 2.2% to 4.8%. Treatment related AEs that reported at more than or equal to 5% for SPN-812 were somnolence, headache, decreased appetite, fatigue and upper abdominal pain.

Results of P302 Phase III trial

On December 20, 2018, we announced positive topline results from the P302 Phase III study of SPN-812 in patients 12 to 17 years old for the treatment of ADHD. The trial was successful in meeting the primary endpoint, demonstrating that SPN-812 at daily doses of 200 mg and 400 mg achieved a statistically significant improvement in the symptoms of ADHD from baseline to end of study as measured by the ADHD-RS-5. Each of the SPN-812 doses tested in the trials was well tolerated.

The study is a randomized, double-blind, placebo controlled, multicenter, parallel group clinical trial in adolescents 12 to 17 years of age diagnosed with ADHD. Each treatment was administered orally once a day over six weeks, including the titration phase of the 400 mg dose group.

A total of 310 patients were randomized across placebo and two doses of SPN-812 (200mg/400mg). The primary objective was to assess the effect of SPN-812 in reducing the symptoms of ADHD in adolescents 12 to 17 years old. The primary outcome measure was the change from baseline to the end of the study in the ADHD-RS-5 total score. Safety and tolerability of SPN-812 were assessed by the monitoring of AEs, clinical laboratory tests, vital signs, ECGs, suicidality and physical examinations. Patients who completed the study were offered the opportunity to continue into an open-label phase that is currently on-going.

At the end of the P302 Study, SPN-812 200 mg and 400 mg doses reached statistical significance compared to placebo in the primary endpoint. Patients receiving SPN-812 200 mg and 400 mg had a 16.0 point change (p=0.0232) and a 16.5 point change (p=0.0091) from baseline, respectively, in the primary endpoint vs. 11.4 for placebo at week 6. This primary result, based on MMRM analysis in the Intent-To-Treat (ITT) population, was confirmed by sensitivity analyses using ANCOVA (200 mg, p=0.0163; 400 mg, p=0.0055).

The study demonstrated fast onset of action, reaching statistical significance for the 400 mg dose as early as week 1 with a p-value of 0.0085, and maintaining statistical significance on a weekly basis through the end of the trial at week 6. Onset of action for the 200 mg dose showed clear differences compared to placebo starting by week 1, reaching statistical significance at week 3, which was sustained through the rest of the trial. Similar to the P301 and P303 studies, at the end of the P302 study, SPN-812 200 mg and 400 mg reached statistical significance compared to placebo on the hyperactivity/impulsivity and inattention subscales of the ADHD-RS-5 scale with p-values ranging from 0.0005 to 0.0424. In addition, SPN-812 200 mg and 400 mg met the CGI-I secondary endpoint with p-values of 0.0042 and 0.0003, respectively, compared to placebo.

Overall, the trial exhibited favorable tolerability and safety profiles with low incidence of AEs across all doses. AEs were mild leading to low discontinuation rates due to AEs of 1.9% to 4.1%. Treatment related AEs that reported at more than or equal to 5% for SPN-812 were somnolence, fatigue, decreased appetite, headache and nausea.

SPN-810 (molindone hydrochloride)

We are developing SPN-810 as a novel treatment for IA in patients who have ADHD. Molindone hydrochloride was previously marketed in the United States as an anti-psychotic drug to treat schizophrenia in patients, under the trade name Moban, albeit at much higher dosages (up to 225mg/day) than we are using in our development program (36 and 54 mg/day). Moban has not been commercially available since 2010 and the FDA has confirmed that the withdrawal from the

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market was not due to issues with safety or efficacy. A generic-equivalent approval is listed in the FDA's Orange Book. Molindone hydrochloride is differentiated from other anti-psychotic drugs in that it is less likely to be associated with weight gain and, in preclinical models, has not caused increases in prolactin levels as seen with other anti-psychotic drugs.

We believe the lower doses tested for the proposed indication of IA in ADHD should be better tolerated than the higher doses approved to treat schizophrenia. If we are successful in developing SPN-810 as a novel treatment for IA in patients who have ADHD, we may then develop the product as a candidate for treating other indications; e.g., patients with IA in autism, PTSD, bipolar disorder, Alzheimer's and other forms of dementia. In the aggregate, we believe the addressable market for SPN-810 is greater than $6.3 billion, including $3.2 billion in ADHD, $0.8 billion in autism and $2.3 billion in PTSD. We are developing IP covering the novel synthesis process for the active ingredient in SPN-810, its novel use in IA and its novel extended release delivery.

SPN-810 Development Program: Phase III Trials

SPN-810 has been granted fast-track designation by the FDA. Our first Phase III clinical trial (P301) was designed under a Special Protocol Assessment (SPA) with the FDA, using a novel measurement scale developed by us. The second Phase III clinical trial (P302), which is also being conducted in children, uses the same trial design of P301 and the same novel measurement scale except that under the SPA, an interim analysis was conducted in the P301 trial. The purpose of the interim analysis was to assess the efficacy of the doses being tested and to allow for optimization of the trial design of both trials. The interim analysis was completed in 2017 and, as a result, we discontinued the 18 mg dose arm. Moving forward, all patients in each of the two trials are randomized to either the 36 mg dose arm or placebo.

The first Phase III trial (P301) has reached its original enrollment target with data originally scheduled to be released in the second quarter of 2019. However, given that the data readout from the second trial (P302) is now expected in the second half of 2019, we have decided to keep enrolling in the P301 trial until data from both trials can be released concurrently instead of sequentially. We believe this change in the plan has no impact on the timing of the NDA filing because the completion of the second Phase III trial (P302) and the generation of data from the adolescent patient population (P503) are now rate-limiting for the NDA filing. We expect to submit the NDA for SPN-810 in the second half of 2020, and to launch it, pending FDA approval, in the second half of 2021.

Patients completing the Phase III trials can continue treatment under our open label extension trial. Enrollment from the P301 and P302 trials into the open label extension trial continues at 90% or higher. On average, a patient in the open label extension study stays on SPN-810 for approximately 10 months, which we believe is an encouraging sign of both tolerability and efficacy of SPN-810.

In addition, patient enrollment began in December 2018 in a Phase III trial for SPN-810 (P503) treating IA in adolescents who have ADHD.

SPN-810 Development Program: Phase II Trials

We completed a Phase IIb multicenter, randomized, double-blind, placebo-controlled trial in the United States in pediatric subjects 6 to 12 years of age diagnosed with ADHD and with IA that is not controlled by optimal stimulant and behavioral therapy. The primary objective of the study was to assess the effect of SPN-810 in reducing IA as measured by the Retrospective-Modified Overt Aggression Scale (R-MOAS) after at least three weeks of treatment. Secondary endpoints included the rate of remission of IA and measurement of the effectiveness of SPN-810 on the Clinical Global Impression (CGI) and ADHD scales as well as evaluation of the safety and tolerability of the drug. Patients who completed the study were offered the opportunity to continue into an open-label phase of six months duration.

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Analysis of treatment was performed using both parametric and non-parametric statistical methods. The parametric method assumes that data are normally distributed. Under this method, mean results of each treatment group at the end of three weeks of treatment were compared to the baseline R-MOAS score for each of the four dose groups (high, medium, low and placebo) using the t-test. The non-parametric method does not assume that data are normally distributed. Under this method, the median results of the change in R-MOAS score from baseline at the end of three weeks of treatment were computed for each of the four dose groups (high, medium, low and placebo). These were compared using the Wilcoxon Rank-sum test. Statistical analyses were performed to compare the median of each of the treatment groups (high, medium, and low versus placebo) at the end of three weeks of treatment. The change in score from baseline to visit 10 was used as the outcome variable.

There was a statistically significant difference between the low dose and placebo ($p=0.031$) and also between the medium dose and placebo ($p=0.024$) at the $\alpha=0.05$ level. There was no statistically significant difference between the high dose and placebo. Both the medium dose and low dose were superior to placebo. These results convinced us that both low and medium doses were effective. This range of doses is being further evaluated in the on-going Phase III clinical trials.

A secondary efficacy variable was the proportion of children whose impulsive aggressive behavior remitted, with remission defined as R-MOAS ≤ 10 at the end of the study. Low and medium doses of SPN-810 showed statistically significant results versus placebo, with the percent of patients who experienced remission of impulsive aggressive behavior of 51.9% ($p=0.009$) and 40.0% ($p=0.043$), respectively.

The CGI results (Severity and Improvement) are consistent with the findings on the R-MOAS scale, in that notable improvement (reduction in severity) occurred primarily in the low dose and medium dose groups. Scores on SNAP-IV Hyperactivity and Impulsivity items did not exhibit statistically significant differences across treatment groups, indicating that efficacy against IA was specific, rather than being efficacious against the underlying ADHD. Numerical trends in SNAP-IV Oppositional Defiant Disorder scores, while not always significant, consistently favored the low dose and medium dose groups over placebo.

SPN-810 was well tolerated throughout the study across all doses. Sedation was the most frequently reported adverse reaction, with two subjects (7%) reporting this event in each of the four treatment groups, including the placebo group. The next most frequently reported adverse reaction was increased appetite with two subjects (7%) reporting this event in each of the three active treatment groups and one subject (3%) in the placebo group.

The two serious AEs that occurred were not drug-related. One patient in the low dose arm and two patients in the medium dose arm had severe AEs that were considered either possibly or definitely related to the drug. Six patients in total discontinued the study because of AEs in the active treatment arms: one in low dose; two in medium dose; and three in the high dose arm. AEs requiring dose reduction were infrequent.

The frequency of AEs associated with extra-pyramidal symptoms was also low and the events were reversible. The data are too sparse to evaluate dose-related aspects of these reports; thus, no clear dose-response relationship can be assessed. SPN-810 exhibited a very good safety and tolerability profile, with low incidence of AEs, and no unexpected, life threatening, or dose-limiting safety issues.

The Phase IIb trial with SPN-810, which included 121 patients, showed that there was no meaningful difference in weight gain between patients treated with SPN-810 and those treated with placebo.

SPN-809 (viloxazine hydrochloride)

SPN-809 is a novel once-daily product candidate for the treatment of depression. SPN-809 incorporates the same active ingredient as SPN-812. We currently have an open investigational new drug application

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(IND) for SPN-809 as a treatment for depression, the indication for which the active ingredient in SPN-809 was approved and marketed in Europe for many years. It was never approved in the U.S., for this indication.

Because SPN-809 contains the same active ingredient as SPN-812, we expect that many of our activities related to the development of SPN-812 will also benefit the development of SPN-809.

SPN-604 (extended release oxcarbazepine for bipolar)

We continue to progress our plans to initiate pivotal Phase III studies for the treatment of bipolar disorder in the second half of 2019. If approved, this would represent the first approval for treatment of bipolar patients with oxcarbazepine in the U.S. Recently, we completed certain activities, including market research and claims database analysis on the use of oxcarbazepine in bipolar patients. We will be using information generated from these activities to finalize plans for the pivotal Phase III trials.

We expect to incur significant research and development expenses related to the continued development of each of our product candidates from 2019 through FDA approval or until the program terminates. We incurred total research and development expense of $89.2 million, $49.6 million and $42.8 million for the years ended December 31, 2018, 2017 and 2016, respectively.

ADHD Competition

Competition in the U.S. ADHD market has increased with the commercial launch of several products in recent years, including the launch of generic versions of branded drugs, such as Adderall XR, Intuniv and Strattera.

Treatment options for ADHD in the U.S. market can be broadly classified as either stimulants or non-stimulants. Shire Plc is one of the leaders in the U.S. ADHD market with four marketed products: Vyvanse, a stimulant drug product launched in 2007; Intuniv, a non-stimulant treatment launched in November 2009; Adderall XR, an extended release stimulant treatment designed to provide once-daily dosing, launched in October 2001; and Mydayis, a stimulant treatment launched in August 2017. Other marketed stimulant products for the treatment of ADHD in the U.S. include the following once-daily formulations: Mydayis, Concerta, Metadate CD, Ritalin LA, Focalin XR, Daytrana, Adzenys XR-ODT, Cotempla XR ODT and Aptensio XR. Other marketed non-stimulants in the U.S. include Strattera and Kapvay.

We are also aware of clinical development efforts by several organizations including Sunovion, Ironshore/Highland and Otsuka to develop additional treatment options for ADHD. Sunovion recently filed its non-stimulant product, dasotraline, with the FDA in September of 2017 for treatment of adults, children and adolescents with ADHD and received a non-approvable letter. In 2018, Ironshore/Highland received FDA approval of Jornay PM, a new stimulant product that is expected to be launched in 2019.

Our Proprietary Technology Platforms

We have a successful track record of developing novel, products by applying proprietary technologies to known drugs to improve existing therapies and to enable the treatment of new indications. Our key proprietary technology platforms include Microtrol, Solutrol and EnSoTrol. These technologies create novel, customized product profiles designed to enhance efficacy, reduce the frequency of dosing, and improve patient compliance and tolerability. We have employed our technologies in the development of a total of ten products that are currently on the market, including Trokendi XR and Oxtellar XR, along with eight products being marketed by our partners. Trokendi XR uses the Microtrol multiparticulate delivery platform and Oxtellar XR uses the Solutrol matrix delivery platform. EnSoTrol was utilized to develop Orenitram, an oral formulation of treprostinil diethanolamine, or treprostinil, which was

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launched by United Therapeutics Corporation in 2014. Microtrol was utilized to develop Mydayis, which was launched by Shire in 2017.

Intellectual Property and Exclusivity

Overview

We have been building and continue to build our IP portfolio relating to our products and product candidates, including Oxtellar XR and Trokendi XR. We seek patent protection, where appropriate, in the U.S. and internationally for our products and product candidates. Our policy is to protect our innovations and proprietary products by, among other things, filing patent applications in the U.S. and abroad, including Europe, Canada and other countries when appropriate. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our technology.

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for the technologies and products we consider important to our business, our ability to defend our patents and our ability to preserve the confidentiality of our trade secrets and operate our business without infringing the patents and proprietary rights of third parties.

We have established and continue to build proprietary positions for Oxtellar XR, Trokendi XR, our pipeline product candidates and our technologies in the U.S. and abroad.

Patents for both Oxtellar XR and Trokendi XR have received numerous challenges, in the form of Paragraph IV Notice Letters and we have filed claims for infringement of our patents against the third-parties. On Oxtellar XR, the Company prevailed in its litigation against the third parties, and therefore, we expect that Oxtellar XR will have patent protection through the expiry of its patents in 2027. On Trokendi XR, the Company entered into settlement agreements that allow third parties to enter the market on January 1, 2023, or earlier under certain circumstances. For more information, please see Part I, Item 3 *Legal Proceedings* contained in this Annual Report on Form 10-K.

Patent Portfolio

Our extended release oxcarbazepine patent portfolio currently includes eleven U.S. patents, eight of which cover Oxtellar XR. We have also obtained two patents each for extended release oxcarbazepine in Europe and Australia, and one patent each in Canada, Japan, China and Mexico. In addition, we have certain pending U.S. patent applications that cover various extended release formulations containing oxcarbazepine. The eight issued U.S. patents covering Oxtellar XR will expire no earlier than 2027. We own all of the issued patents and the pending patent applications.

In addition to the patents and patent applications relating to Oxtellar XR, we currently have nine U.S. patents that cover Trokendi XR. We have one patent issued each in Mexico, Australia, Japan and Canada for extended release topiramate. We also have two patents issued in Europe for extended release topiramate. The nine issued U.S. patents covering Trokendi XR will expire no earlier than 2027. We own all of the issued patents and pending patent applications.

Our patent portfolio also contains patent applications relating to our other pipeline products.

With regard to our SPN-810 product candidate, we are developing an IP position covering the novel process of synthesis of the active ingredient, its novel use in IA and novel formulation. We have four families of pending U.S. non-provisional and foreign counterpart patent applications relating to our SPN-810 product candidate. Patents, if issued, could have terms expiring from 2029 to 2033. We have

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two patents issued in the U.S., and one patent issued each in Canada, Mexico, Europe, Australia and Japan, covering modified release formulations of molindone hydrochloride. In another patent family, covering the novel process of synthesis of the active ingredient, we have four patents issued in the U.S, two patents issued in Japan, and one patent issued each in Europe, Mexico, and Australia. The third patent family, covering use of molindone hydrochloride in treating aggression, includes three patents issued in the U.S., two patents issued each in Japan and Austrailia, and one patent issued in Canada. We own all of the issued and pending patent applications.

With regard to our SPN-812 product candidate, we have three families of pending U.S. non-provisional and foreign counterpart patent applications. Patents, if issued, could expire from 2029 to 2033. We have one patent issued each in Europe and Canada, covering a method of treating ADHD using viloxazine. In another family, covering the novel process of active ingredient synthesis, we have four patents issued in the U.S., five patents issued in Mexico, and one patent issued each in Europe, Japan, Canada and Australia. We have three patents issued in the U.S. covering modified release formulations of viloxazine and one patent issued in Japan, Mexico and Australia. We own all of the issued patents and the pending patent applications.

The U.S. patent system permits the filing of provisional and non-provisional patent applications. A non-provisional patent application is examined by the United States Patent and Trademark Office (USPTO) and can mature into a patent once the USPTO determines that the claimed invention meets the standards for patentability. The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the U.S., a patent's term may be lengthened by patent term adjustment (PTA), which compensates a patentee for administrative delays by the USPTO in granting a patent. In view of a recent court decision, the USPTO is under greater scrutiny regarding its calculations of PTAs because the USPTO erred in calculating the PTA in that case, which resulted in denying the patentee a portion of the patent term to which it was entitled. Alternatively, a patent's term may be shortened if a patent is terminally disclaimed over another patent.

In evaluating the patentability of a claimed invention, the filing date of a non-provisional patent application is used by the USPTO to determine what information is prior art. If certain requirements are satisfied, a non-provisional patent application can claim the benefit of the filing date of an earlier filed provisional patent application. As a result, the filing date accorded by the provisional patent application may supersede information that otherwise could preclude the patentability of an invention.

The term of a patent that covers an FDA-approved drug may also be eligible for patent term extension (PTE), which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Amendments, permits a PTE of up to five years beyond the expiration of the patent. The length of the PTE is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our pharmaceutical products receive FDA or other regulatory approval, we may be able to apply for PTEs on patents covering those products. Depending upon the timing, duration and specifics of FDA approval of our SPN-810 and SPN-812 product candidates and issuance of a U.S. patent, we may obtain a U.S. patent that is eligible for limited patent term restoration.

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Other Intellectual Property Rights

We seek trademark protection in the U.S. and internationally where available and when appropriate. We have filed for trademark protection for several marks, which we use in connection with our pharmaceutical research and development collaborations as well as with products. We are the owner of various U.S. federal trademark registrations (®) and registration applications ( ), including the following marks referred to in this Annual Report on Form 10-K pursuant to applicable U.S. intellectual property laws: "Supernus®," "Microtrol®," "Solutrol®," "Trokendi XR®," "Oxtellar XR®," and the registered Supernus Pharmaceuticals logo.

From time to time, we may find it necessary or prudent to obtain licenses from third party IP holders. Where licenses are readily available at reasonable cost, such licenses are considered a normal cost of doing business. In other instances, however, we may use the results of freedom-to-operate inquiries and internal analyses to guide our early-stage research away from areas where we are likely to encounter obstacles in the form of third party IP. For example, where a third party holds relevant IP and is a direct competitor, a license might not be available on commercially reasonable terms or at all. We strive to identify potential third party IP issues in the early stages of our research programs in order to minimize the cost and disruption of resolving such issues.

To protect our competitive position, it may be necessary to enforce our patent rights through litigation against infringing third parties. We presently have a lawsuit pending against TWi Pharmaceuticals Inc. to enforce our patent rights concerning Oxtellar XR patents. See Part I, Item 3 *Legal Proceedings*. Litigation to enforce our own patent rights is subject to uncertainties that cannot be quantified in advance. In an adverse outcome in litigation, we could be prevented from commercializing a product or using certain aspects of our technology platforms if patent infringement claims are asserted against us. This could have a material adverse effect on our business. In addition, litigation involving our patents carries the risk that one or more of our patents will be held invalid (in whole or in part, on a claim-by-claim basis) or held unenforceable. Such an adverse court ruling could allow third parties to commercialize products or use technologies that are similar to ours, and then compete directly with us, without payment to us. See Part I, Item 1A Risk Factor: "If we are sued for infringing intellectual property rights of third parties, it could be costly and time consuming to defend such a suit. An unfavorable outcome in that litigation could have a material adverse effect on our business."

In-Licensing Arrangements

Afecta Pharmaceuticals, Inc.

We have two license agreements with Afecta Pharmaceuticals, Inc. (Afecta) pursuant to which we obtained exclusive worldwide rights to selected product candidates, including an exclusive license to SPN-810. We may pay up to $300,000 upon the achievement of certain milestones. If a product candidate is successfully developed and commercialized, we will be obligated to pay royalties to Afecta at a rate in the low-single digits, based on worldwide net product sales.

Rune HealthCare Limited

We have a purchase and sale agreement with Rune HealthCare Limited (Rune) where we obtained the exclusive worldwide rights to a product concept from Rune for SPN-809. If we receive approval to market and sell any products covered by the agreement, we will be obligated to pay royalties to Rune at a rate in the low-single digits, based on worldwide net sales.

SPN-817

We obtained worldwide rights, excluding certain markets in Asia where rights have been out-licensed, to SPN-817, which has received an Orphan Drug designation from the FDA for the treatment of

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Dravet Syndrome, a severe form of childhood epilepsy. These rights were obtained through our acquisition of Biscayne. We may be obligated to pay additional payments if certain milestones are met including $73 million contingent on achieving certain development milestones and up to $95 million contingent upon achieving certain sales milestones. In addition, we will be obligated to pay a low single digit royalty on net sales to Biscayne and any applicable royalties to third parties for the use of in-licensed IP. The maximum combined royalty we will pay to all parties is approximately 12% depending on the IP covering the marketed product and the applicable tiered sales levels.

Confidential Information and Inventions Assignment Agreements

We require our employees, temporary employees and consultants to execute confidentiality agreements upon the commencement of employment, consulting or collaborative relationships with us. These agreements provide that all confidential information developed or made known during the course of the relationship with us be kept confidential and not disclosed to third parties except in specific circumstances. The agreements provide that all inventions resulting from work performed for us or relating to our business and conceived or completed by the individual during employment or assignment, as applicable, shall be our exclusive property to the extent permitted by applicable law.

We seek to protect our products, product candidates and our technologies through a combination of patents, trade secrets, proprietary know-how, FDA exclusivity and contractual restrictions on disclosure.

Government Regulation

U.S. Review and Approval Processes

The results of product development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the drug, proposed labeling and other relevant information are submitted to the FDA as part of the approval process for a new drug, filed as an NDA. The NDA requests approval to market the product. The submission of an NDA is subject to the payment of a substantial user fee, although a waiver of such fee may be obtained under certain limited circumstances.

Our activities encompass two types of NDAs: the Section 505(b)(1) NDA (Full NDA) and the Section 505(b)(2) NDA. A Section 505(b)(1), which is a Full NDA, must contain all pertinent information and full reports of investigations conducted by the applicant to demonstrate the safety and effectiveness of the drug and complete preclinical, clinical and manufacturing information. The 505(b)(2) regulatory approval process is designed to allow for potentially expedited, lower cost and lower risk regulatory approval based on previously established safety, efficacy and manufacturing information on a drug that has been already approved by the FDA for the same or a different indication. For a 505(b)(2) application, the FDA permits the submission of an NDA where at least some of the information required for approval comes from clinical trials not conducted by or for the applicant and for which the applicant has not obtained a right of reference. The FDA interprets Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) to permit the applicant to rely upon the FDA's previous findings of safety and effectiveness for an approved product. The FDA requires submission of information needed to support any changes to a previously approved drug, such as published data or new studies conducted by the applicant, including bioavailability or bioequivalence studies, or clinical trials demonstrating safety and effectiveness. The FDA may then approve the new product candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

We will need to file a Section 505(b)(1) NDA for SPN-812 and for certain products in the future. A 505(b)(1) NDA for SPN-812 carries a higher degree of regulatory approval risk than a 505(b)(2) NDA. In addition, a requirement for more extensive testing and development for some other reason can adversely impact our ability to compete with alternative products that arrive on the market more

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quickly than our product candidate. In addition, the time and financial resources required to obtain FDA approval for SPN-812 could substantially and materially increase. After Supernus gains one approval for SPN-812, additional indications may be considered for NDA applications using the 505(b)(2) regulatory pathway. The FDA may not approve of our filing under Section 505(b)(2) for SPN-812 for other indication(s), such as PTSD, and therefore would require a full NDA filing. In such a case, the time and financial resources required to obtain approval could also significantly increase.

In addition, under the Pediatric Research Equity Act of 2003 (PREA), which was reauthorized under the Food and Drug Administration Safety and Innovation Act of 2012, an NDA must contain, *a priori*, or propose clinical work that supports the product's use in all relevant pediatric subpopulations. The FDA may grant deferrals for submission of data or full or partial waivers of the data requirements.

Pursuant to the FDA's approval of Oxtellar XR, we committed to conduct four pediatric post-marketing studies; however, the FDA granted a waiver for the pediatric study requirements for ages from birth to one month and a deferral for submission of post-marketing assessments for children one month to six years of age.

Pursuant to the FDA's approval of Trokendi XR, the FDA granted a deferral for submission of post-marketing pediatric studies in the following categories: (1) adjunctive therapy in partial onset seizures (POS) for children one month to less than six years of age, (2) initial monotherapy in POS and PGTC for children two years to less than ten years of age, and (3) adjunctive therapy in PGTC and adjunctive therapy in Lennox-Gastaut Syndrome from two years to less than six years of age.

Since our product approvals, we have gained knowledge about our abilities to create formulations and successfully execute programs that would enable us to meet our deferred pediatric commitments. We have identified a need to renegotiate the commitments made at the time of NDA approvals for both Oxtellar XR and Trokendi XR. Supernus is actively interfacing with the FDA on these programs and these commitments.

Section 505(b)(2) New Drug Applications

To the extent that a Section 505(b)(2) NDA relies on clinical trials conducted for a previously approved drug product or the FDA's prior findings of safety and effectiveness for a previously approved drug product, the Section 505(b)(2) applicant must submit patent certifications in its Section 505(b)(2) application with respect to any patents for the approved product on which the application relies that are listed in the FDA's publication, Approved Drug Products with Therapeutic Equivalence Evaluations, commonly referred to as the Orange Book. Specifically, the applicant must certify for each listed patent that either: (1) the required patent information has not been filed; or (2) the listed patent has expired; or (3) the listed patent has not expired, but will expire on a particular date and approval is not sought until after patent expiration; or (4) the listed patent is invalid, unenforceable or will not be infringed by the proposed new product. A certification that the new product will not infringe the previously approved product's listed patent or that such patent is invalid or unenforceable is known as a Paragraph IV certification.

If the applicant does not challenge one or more listed patents through a Paragraph IV certification, the FDA will not approve the Section 505(b)(2) NDA application until all the listed patents claiming the referenced product have expired. Further, the FDA also will not approve, as applicable, a Section 505(b)(2) NDA application until any non-patent exclusivity, such as, for example, five-year exclusivity for obtaining approval of an NCE, or three year exclusivity for an approval based on new clinical trials, or pediatric exclusivity, listed in the Orange Book for the referenced product, has expired.

A section 505(b)(2) NDA applicant must send notice of the Paragraph IV certification to the owner of the referenced NDA for the previously approved product and relevant patent holders within 20 days

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after the Section 505(b)(2) NDA has been accepted for filing by the FDA. If the relevant patent holder elects to initiate litigation, the Section 505(b)(2) applicant may invest a significant amount of time and expense in the development of its product only to be subject to significant delay and patent litigation before its product may be commercialized. Alternatively, if the NDA applicant or relevant patent holder does not file a patent infringement lawsuit within the specified 45 day period, the FDA may approve the Section 505(b)(2) application at any time.

Notwithstanding the approval of many products by the FDA pursuant to Section 505(b)(2) over the last few years, some pharmaceutical companies and others have objected to the FDA's interpretation of Section 505(b)(2). If the FDA changes its interpretation of Section 505(b)(2), or if the FDA's interpretation is successfully challenged in court, this could delay or even prevent the FDA from approving any Section 505(b)(2) NDA that we submit.

If a product receives regulatory approval, the approval may be limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may require Phase IV testing which involves clinical trials designed to further assess a drug's safety and efficacy after NDA approval, and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized.

Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, some of our U.S. patents may be eligible for limited PTE under the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent term restoration of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent and within sixty days of approval of the drug. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

Market exclusivity provisions under the FDCA can also delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the U.S. to the first applicant to gain approval of an NDA for an NCE. A drug is an NCE if the FDA has not previously approved any other new drug containing the same active pharmaceutical ingredient (API) or active moiety, which is the molecule or ion responsible for the therapeutic action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application (ANDA) or a Section 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. As an alternative to submission via 505(b)(2) approval, an applicant may choose to submit a full Section 505(b)(1) NDA. Such an NDA applicant would be required to conduct its own preclinical and adequate, well-controlled clinical trials to demonstrate safety and effectiveness, without reference to other clinical trials or data.

The FDCA also provides three years of marketing exclusivity for an NDA, Section 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations (other than bioavailability studies) that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application. Such clinical trials may, for example, support new indications, dosages, routes of

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administration or strengths of an existing drug, or for a new use, if the new clinical investigations that were conducted or sponsored by the applicant are determined by the FDA to be essential to the approval of the application. This exclusivity, sometimes referred to as clinical investigation exclusivity, prevents the FDA from approving an application under Section 505(b)(2) for the same conditions of use associated with the new clinical investigations before the expiration of three years from the date of approval. Such three-year exclusivity, however, would not prevent the approval of another application if the applicant submits a Section 505(b)(1) NDA and has conducted its own adequate, well-controlled clinical trials demonstrating safety and efficacy, nor would it prevent approval of a Section 505(b)(2) product that did not incorporate the exclusivity-protected changes of the approved drug product. The FDCA, FDA regulations and other applicable regulations and policies provide incentives to manufacturers to create modified, non-infringing versions of a drug to facilitate the approval of an ANDA or other application for generic substitutes.

Pediatric exclusivity is another type of exclusivity granted in the U.S. Pediatric exclusivity, if granted, provides an additional six months of exclusivity to be attached to any existing exclusivity (e.g., three or five year exclusivity) or patent protection for a drug. This six month exclusivity, which runs from the end of other exclusivity protection or patent delay, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial. The current pediatric exclusivity provision was reauthorized in September 2007.

Customers

The majority of our product sales are to wholesalers and distributors who, in turn, sell the products to pharmacies, hospitals and other customers, including federal and state entities. Three customers, AmerisourceBergen Drug Corporation, Cardinal Health, Inc. and McKesson Corporation, individually accounted for more than 30% of our total revenue in 2018, and collectively accounted for 98% of our total revenue in 2018.

Employees

As of December 31, 2018, we employed 448 full-time employees; 104 employees are engaged in research and development activities and 344 employees are engaged in selling, general and administrative activities. We consider relations with our employees to be good. None of our employees is represented by a labor union.

Internet Information

Our website is *www.supernus.com*. Through a link on the Investor Relations portion of our website, you can access our filings with the Securities and Exchange Commission (SEC). You may request, orally or in writing, a copy of these filings, which will be provided to you at no cost, by contacting our investor relations department at our principal executive offices, which are located at 1550 East Gude Drive, Rockville, Maryland 20850. Information contained on our website is not a part of this Annual Report on Form 10-K.

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ITEM 1A. RISK FACTORS.

Investing in our common stock involves a high degree of risk. Before making an investment decision, you should carefully consider the risks described below with all of the other information we include in this report and the additional information in the other reports we file with the Securities and Exchange Commission (the "SEC" or the "Commission"). These risks may result in material harm to our business, our financial condition, and results of operations. In this eventuality, the market price of our common stock may decline and you could lose part or all of your investment.

Risks Related to Our Business and Industry

We are dependent on the commercial success of Oxtellar XR and Trokendi XR.

A substantial amount of our resources are focused on maintaining and/or expanding the revenue generated by our approved products in the U.S., Oxtellar XR and Trokendi XR.

Our ability to generate significant product revenue from sales of Oxtellar XR and Trokendi XR in the near term will depend on, among other things, our ability to:

- Defend our patents, intellectual property and products from competition, both branded and generic;
- Maintain commercial manufacturing arrangements with third-party manufacturers;
- Produce, through a validated process, sufficiently large quantities of inventory of our products to meet demand;
- Continue to maintain a wide variety of internal sales, distribution and marketing capabilities sufficient to sustain and grow revenue;
- Continue to maintain and grow widespread acceptance of our products from physicians, health care payors, patients, pharmacists and the medical community;
- Properly price and obtain adequate reimbursement coverage of these products by governmental authorities, private health insurers, managed care organizations and other third-party payors;
- Maintain compliance with ongoing FDA labeling, packaging, storage, advertising, promotion, recordkeeping, safety and other post-market requirements;
- Obtain approval from the FDA to expand the labeling of our approved products for additional indications;
- Adequately protect against and effectively respond to any claims by holders of patents and other IP rights that our products infringe their rights; and
- Adequately protect against and effectively respond to any unanticipated adverse effects or unfavorable publicity that develops with respect to our products, as well as respond to the emergence of new or existing competitive products, including therapeutically equivalent products, which may be proven to be more clinically effective and cost-effective.

There are no guarantees that we will be successful in completing these tasks. We will need to continue investing substantial financial and management resources to maintain our commercial sales and marketing infrastructure and to recruit and train qualified marketing, sales and other personnel. In addition, we have expressed certain long term revenue expectations. If we cannot achieve those revenue expectations with respect to Oxtellar XR and Trokendi XR, this could result in a material adverse impact on our anticipated revenue, earnings and liquidity.

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Increases in sales of Oxtellar XR or Trokendi XR may slow for a variety of reasons, including competing products or safety issues. If we are not successful in broadening the current commercial acceptance of either Oxtellar XR or Trokendi XR, our business would be harmed.

Any increase in sales of Oxtellar XR and Trokendi XR will be dependent on several factors, including our ability to educate physicians and to increase physician awareness and acceptance of the benefits and cost-effectiveness of our products relative to competing products. Our ability to increase market acceptance of any of our products or gain market acceptance of approved product candidates among physicians, patients, health care payors and the medical community will depend on a number of factors, including:

Acceptable evidence of safety and efficacy;

Relative convenience and ease of administration;

The prevalence, nature, and severity of any adverse side effects;

Availability of alternative treatments including branded and generic products; and

Pricing and cost effectiveness.

In addition, Oxtellar XR and Trokendi XR are subject to continual review by the FDA. We cannot provide assurance that newly discovered or reported safety issues will not arise. With the use of any marketed drug by a wider patient population, serious AEs may occur from time to time that initially do not appear to be related to the drug itself. Any safety issues could cause us to suspend or cease marketing of our approved products, cause us to modify how we market our approved products, subject us to substantial liabilities and adversely affect our revenues and financial condition. In the event of a withdrawal of either Oxtellar XR or Trokendi XR from the market, our revenues would decline significantly and our business would be seriously harmed and could fail.

We could be involved in lawsuits to protect or enforce our patents, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. For example, we were involved in several matters related to Paragraph IV Certification Notice Letters that we received in connection with our products and our collaborators' products. In connection with an ANDA (Abbreviated New Drug Application), a Paragraph IV Certification Notice Letter notifies the FDA that one or more patents listed in the FDA's Orange Book is alleged to be invalid, unenforceable or will not be infringed by the ANDA product. These matters included claims related to Oxtellar XR, and are discussed in Part I, Item 3 *Legal Proceedings*.

In any infringement proceeding, a court may decide that a patent of ours is not valid or enforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent application at risk of not issuing.

Interference proceedings brought by the USPTO (U.S. Patent and Trademark Office) may be necessary to determine the priority of inventions with respect to our patents and patent applications or those of our collaborators. An unfavorable outcome could require us to cease using the technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if a prevailing party does not offer us a license on terms that are acceptable to us or at all. Litigation or interference proceedings may fail. Even if successful, litigation may result in substantial costs and distraction of our management and other employees. We may not be able to prevent, alone or with our collaborators,

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misappropriation of our proprietary rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of 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, there could be public announcements of the results of hearings, motions or other interim proceeding or developments. If securities analysts or investors perceive these results to be negative, or perceive that the presence or continuation of these cases creates a level of uncertainty regarding our ability to increase or sustain products sales, it could have a substantial adverse effect on the price of our common stock. There can be no assurance that our product candidates will not be subject to the same risks.

We are dependent on obtaining regulatory approval of our product candidates and for additional indications for existing products.

Our ability to successfully commercialize any of our product candidates and to obtain additional indications for existing products will depend on, among other things, our ability to:

- Successfully complete our clinical trials;
- Receive marketing approvals from the FDA;
- Produce, through a validated process, sufficiently large quantities of our product candidates to permit successful clinical development and commercialization;
- Establish commercial manufacturing arrangements with third-party manufacturers;
- Build and maintain strong sales, distribution and marketing capabilities sufficient to commercially launch our product candidates;
- Secure acceptance of our product candidates from physicians, health care payors, pharmacies, wholesalers, patients and the medical community; and
- Manage our spending as costs and expenses increase due to undertaking clinical trials and commercially launching product candidates.

There are no guarantees that we will be successful in completing these tasks. If we are unable to successfully complete these tasks, we may not be able to commercialize any of our product candidates in a timely manner, or at all, in which case we may be unable to maximize our revenues. In addition, if we experience unanticipated delays or problems, development costs could substantially increase and our business, financial condition and results of operations would likely be adversely affected.

Our clinical trials for our product candidates may fail to demonstrate acceptable levels of safety, efficacy or any other requirements, which could prevent or significantly delay regulatory approval.

We may be unable to sufficiently demonstrate the safety and efficacy of our product candidates to obtain regulatory approval. We must demonstrate, with substantial evidence gathered in well-controlled studies and to the satisfaction of the relevant regulatory authorities, that each product candidate is safe and effective for use in the target indication. We may be required to conduct or perform additional studies or trials to adequately demonstrate safety and efficacy, which could prevent or significantly delay our receipt of regulatory approval, increase clinical costs, and ultimately delay or otherwise impair the commercialization of that product candidate.

Any product candidate that we in-license or acquire may require additional development prior to commercial sale, including formulation development, extensive clinical testing and approval by the FDA

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and applicable foreign regulatory authorities. All product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities.

In addition, the results from the trials that we have completed for our product candidates may not be replicated in future trials. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced development, even after promising results in earlier trials. If our product candidates are not shown to be safe and effective, our clinical development programs might be terminated.

Delays or failures in the completion of clinical development of our product candidates would increase our costs and delay or limit our ability to generate revenues.

Delays or failures in the completion of clinical trials for our product candidates could significantly raise our product development costs. We do not know whether current or planned trials will be completed on schedule, if at all. The commencement and completion of clinical development can be delayed or halted for a number of reasons, including:

- Difficulties in obtaining regulatory approval to commence a clinical trial or in complying with conditions imposed by a regulatory authority regarding the scope or term of a clinical trial;
- Delays in reaching or failure to reach agreement on acceptable terms with prospective Clinical Research Organization (CRO) trial sites and investigators, the terms of which can be subject to extensive negotiation and may vary significantly;
- Insufficient or inadequate supply or quantity of a product candidate for use in trials;
- Difficulties obtaining Investigational Research Board (IRB) or ethics committee approval to conduct a trial at a prospective site;
- Challenges recruiting and enrolling patients to participate in clinical trials for a variety of reasons, including competition from other programs for the treatment of similar conditions;
- Severe or unexpected drug-related side effects experienced by patients in a clinical trial;
- Difficulty retaining patients who have enrolled in a clinical trial but may be prone to withdraw due to side effects from the therapy, lack of efficacy or personal issues;
- Temporary cessation of clinical trials (clinical holds); or
- Clinical trials may be delayed as a result of ambiguous or negative interim results.

Clinical trials may be suspended or terminated by us, at a trial site by a Data Safety Monitoring Board (DSMB) or ethics committee overseeing the clinical trial, the FDA, or other regulatory authorities due to a number of factors, including:

- Failure to conduct the clinical trial in accordance with regulatory requirements or the trial protocols;
- Observations during inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities that ultimately result in the imposition of a delay or clinical hold;

Unforeseen safety issues; or

Lack of adequate funding to continue the trial.

Failure to conduct the clinical trial in accordance with regulatory requirements or the trial protocols may result in the inability to use the trial data to support product approval. Changes in regulatory requirements and guidance may occur, and we may need to amend clinical trial protocols to reflect

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these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs or ethics committees for reexamination, which may adversely impact the costs, timing and/or successful completion of a clinical trial.

In addition, many of the factors that cause or lead to a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. If we experience delays in completion of, or if we terminate any of our clinical trials, our ability to obtain regulatory approval for our product candidates may be materially harmed, and our commercial prospects and ability to generate product revenues diminished.

Our products and product candidates may cause undesirable side effects or have other characteristics that limit their commercial potential, delay or prevent their regulatory approval.

Undesirable side effects caused by any of our product candidates could cause us or regulatory authorities to interrupt, delay or halt development and could result in the denial of regulatory approval by the FDA or other regulatory authorities, and result in potential product liability claims. Undesirable side effects caused by any of our products could cause regulatory authorities to temporarily or permanently halt product sales, which could have a material adverse effect on our business as a whole.

Immediate release oxcarbazepine and topiramate products, which use the same APIs (Active Product Ingredient) as Oxtellar XR and Trokendi XR, are known to cause various side effects, including but not limited to dizziness, paresthesia, headaches, cognitive deficiencies such as memory loss and speech impediment, digestive problems, somnolence, double vision, gingival enlargement, nausea, weight gain, oral malformation birth defects, visual field defects, infant small for gestational age and fatigue. The use of Oxtellar XR and Trokendi XR may cause similar side effects as compared to their reference products, or may cause additional or different side effects.

Products that were or are currently on the market and use the same API as our product candidates, SPN-810, SPN-812 (drug products), SPN-817 (dietary supplements) and SPN-604, were known to cause various side effects, including but not limited to drowsiness, depression, hyperactivity, euphoria, extrapyramidal reactions, nausea, headache, diarrhea, vomiting, sleep difficulties, agitation, exacerbation of anxiety, sleepiness, mouth dryness, tachycardia, constipation and urinary difficulties. The labels for those products also included precautions and warnings about, among other things, tardive dyskinesia, neuroleptic malignant syndrome, elevation of prolactin levels, convulsive events in patients that are treated for or have a prior history of epilepsy, inhibition of hepatic metabolism of certain drugs, risk of suicide before antidepressant clinical improvement, need for monitoring patients with cardiac, hepatic or renal insufficiency, or patients at risk for angle-closure glaucoma. The use of SPN-810, SPN-812, SPN-817 and SPN-604 may cause similar side effects as compared to these reference products, or may cause additional or different side effects.

If our products cause side effects or if any of our product candidates receive marketing approval, and we or others later identify undesirable side effects caused by our products or product candidates, a number of potentially significant negative consequences could result, including:

- Regulatory authorities may withdraw approval of the product candidate or otherwise require us to take the approved product off the market;
- Regulatory authorities may require additional warnings, or a narrowing of the indication, on the product label;
- We may be required to create a medication guide outlining the proper use of the medication and risks of side effects, for distribution to patients;
- We may be required to modify the product in some way;

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Regulatory authorities may require us to conduct additional clinical trials or costly post-marketing testing and surveillance to monitor the safety or efficacy of the product;

Sales of approved products may decrease significantly;

We could be sued and held liable for harm caused to patients; or

Our reputation may suffer.

Any of these events could prevent us from achieving or maintaining the commercial success of our products and product candidates and could substantially increase commercialization costs.

We may not be able to effectively market and sell our product candidates, if approved, in the U.S.

We plan on building our sales and marketing capabilities in the U.S. to commercialize our product candidates, if approved. We will build such capabilities by investing significant amounts of financial and management resources. Furthermore, the cost of establishing and maintaining marketing and sales capabilities may not be economically justifiable in light of the revenues generated by any of our product candidates.

If we are unable to establish and maintain adequate sales and marketing capabilities for our product candidates or are unable to do so in a timely manner, we may not be able to generate sufficient product revenues from these product candidates to be profitable.

Final marketing approval of any of our product candidates or additional indications for existing products by the FDA or other regulatory authorities may be delayed, limited, or denied, any of which would adversely affect our ability to generate operating revenues.

Our business depends on the successful development and commercialization of our product candidates. We are not permitted to market any of our product candidates in the U.S. until we receive approval of an NDA from the FDA, or, in any foreign jurisdiction, from the requisite authority. Satisfaction of regulatory requirements typically takes many years, is dependent upon the type, complexity and novelty of the product and requires the expenditure of substantial resources. We cannot predict whether or when we will obtain regulatory approval to commercialize our product candidates and we cannot, therefore, predict the timing of any future revenues from these product candidates.

The FDA has substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate or a prior approval supplement for many reasons. For example, the FDA:

Could reject or delay the marketing application for an NCE;

Could determine that we cannot rely on Section 505(b)(2) for any of our product candidates;

Could determine that the information provided by us was inadequate, contained clinical deficiencies or otherwise failed to demonstrate the safety and effectiveness of any of our product candidates for any indication;

May not find the data from bioequivalence studies and/or clinical trials sufficient to support the submission of an NDA or to obtain marketing approval in the U.S., including any findings that the clinical and other benefits of our product candidates outweigh their safety risks;

May disagree with our trial design or our interpretation of data from preclinical studies, bioequivalence studies and/or clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our trials, the outcome and measurement scale used in the trials, and the clinical protocols whether with or without a special protocol assessment process;

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May determine that we have identified the wrong reference listed drug or drugs or that approval of our Section 505(b)(2) application of our product candidate is blocked by patent or non-patent exclusivity of the reference listed drug or drugs;

May identify deficiencies in the manufacturing processes or facilities of third-party manufacturers with which we enter into agreements for the supply of raw materials, including the API or manufactured product candidates used in our product candidates, wherein those deficiencies may result in interruption in the ability to supply product;

May approve our product candidates for fewer or more limited indications than we request, or may grant approval contingent on the performance of costly post-approval clinical trials;

May change its approval policies or adopt new regulations; or

May not approve the labeling claims that we believe are necessary or desirable for the successful commercialization of our product candidates, or may approve them with warnings and precautions that could limit the acceptance of our product candidates and their success

May not approve the addition of new indications to the label of our existing products.

Notwithstanding the approval of many products by the FDA pursuant to Section 505(b)(1) and 505(b)(2), over the last few years some pharmaceutical companies and others have objected to the FDA's interpretation of Section 505(b)(2). If the FDA changes its interpretation of Section 505(b)(2), or if the FDA's interpretation is successfully challenged in court, this could delay or even prevent the FDA from approving any Section 505(b)(2) application that we submit. Any failure to obtain regulatory approval of our product candidates would significantly limit our ability to generate revenues, and any failure to obtain such approval for all of the indications and labeling claims we deem desirable could reduce our potential revenues.

We are subject to uncertainty relating to payment or reimbursement policies which, if not favorable for our products or product candidates, could hinder or prevent our commercial success.

Our ability or our collaborators' ability to successfully commercialize our products, including Oxtellar XR and Trokendi XR and our product candidates, will depend in part on the coverage and reimbursement levels set by governmental authorities, private health insurers, managed care organizations and other third-party payors. As a threshold for coverage and reimbursement, third-party payors generally require that drug products be approved for marketing by the FDA. Third-party payors also are increasingly challenging the effectiveness of and prices charged for medical products and services. Government authorities and third-party payors have attempted to control costs, in some instances, by limiting coverage and the amount of reimbursement for particular medications or encouraging the use of lower-cost generic products. We cannot be sure that reimbursement will be available for any of the products that we develop and, if reimbursement is available, the level of reimbursement. Moreover, that level of reimbursement may change over time as a result of decisions made by payors. Reduced or partial payment or reduced reimbursement coverage could make our products or product candidates, including Oxtellar XR and Trokendi XR, less attractive to patients and prescribing physicians. We also may be required to sell our products or product candidates at a significant discount, which would adversely affect our ability to realize an appropriate return on our investment in our products or product candidates or to maintain profitability.

We expect that private insurers and managed care organizations will consider the efficacy, cost effectiveness and safety of our products or product candidates, including Oxtellar XR and Trokendi XR, in determining whether to approve reimbursement for such products or product candidates and at what level. Moreover, they will consider the efficacy and cost effectiveness of comparable or competitive products in making reimbursement decisions for our products. Because each third-party payor individually approves payment or reimbursement, obtaining these approvals can be a time

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consuming and expensive process that could require us to provide scientific or clinical support for the use of each of our products or product candidates separately to each third-party payor. In some cases, it could take several months or years before a particular private insurer or managed care organization reviews a particular product. We may ultimately be unsuccessful in obtaining coverage. Our competitors may, as well as more extensive existing business relationships with third-party payors relating to their products. Our business would be materially adversely affected if we do not receive approval for reimbursement of our products or product candidates from private insurers on a timely or satisfactory basis. Our products and product candidates may not be considered cost-effective, and coverage and reimbursement may not be available or sufficient to allow us to sell our products or product candidates on a profitable basis. Our business would also be adversely affected if private insurers, managed care organizations, the Medicare program or other reimbursing bodies or payors limit the indications for which our products or product candidates will be reimbursed.

In some foreign jurisdictions, particularly Canada and Europe, the pricing of prescription pharmaceuticals is subject to strict governmental control. In these countries, pricing negotiations with governmental authorities can take six to 12 months or longer after the receipt of regulatory approval and product launch. To obtain favorable reimbursement for the indications sought or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our products or product candidates, if approved, to other available therapies. If reimbursement for our products or product candidates is unavailable in any country in which reimbursement is sought, limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed, and could be unprofitable.

In addition, many managed care organizations negotiate the price of products and establish formularies which establish pricing and reimbursement levels. Exclusion of a product from a formulary can lead to its sharply reduced usage in the managed care organization's patient population. If our products or product candidates are not included within an adequate number of formularies or at adequate payment or reimbursement levels, or if those policies increasingly favor generic products, our market share and gross margins could be negatively affected. This would have a material adverse effect on our overall business and financial condition.

We expect to experience pricing pressures due to potential healthcare reforms discussed elsewhere in this Annual Report on Form 10-K, as well as due to cost control measures instituted by health maintenance organizations.

Our failure to successfully develop and market our product candidates would impair our ability to grow.

As part of our growth strategy, we intend to develop and market additional product candidates. We may spend several years completing the development of a particular current or future internal product candidate, during which process we can experience failure at any stage. The product candidates to which we allocate our resources, even if approved, may not be commercially successful. In addition, because our internal research capabilities are limited, we may be dependent upon pharmaceutical companies, academic scientists and other researchers to sell or license products or technology to us. The success of this strategy depends partly upon our ability to identify, select, discover and acquire promising pharmaceutical product candidates and approved products.

We may be unable to acquire product candidates or products

The process of proposing, negotiating and implementing a license or acquiring a product candidate or approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing and sales resources, may compete with us for the license or the product candidate or approved product. We have limited resources, including financial resources, to identify and execute the acquisition or in-licensing of third-party products, businesses and technologies and to integrate

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them into our current infrastructure. Moreover, we may devote resources to potential acquisitions or in-licensing opportunities wherein those transactions are never consummated, or we may fail to realize the anticipated benefits of such efforts. We may not be able to acquire the rights to additional product candidates on terms that we find acceptable, or at all.

In addition, future acquisitions may entail numerous operational and financial risks, including:

- Exposure to unknown liabilities;
- Disruption of our business and diversion of our management's time and attention to develop acquired products or technologies;
- Incurring substantial debt or dilutive issuances of securities or depletion of cash to pay for acquisitions;
- Incurring higher than expected acquisition, integration, and operating costs;
- Difficulty in combining the operations and personnel of any acquired businesses with our operations and personnel;
- Impairing relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- An inability to retain and/or motivate key employees of any acquired businesses.

We rely on and will continue to rely on outsourcing arrangements for certain of our critical activities, including clinical research of our product candidates, manufacturing of our compounds and product candidates beyond Phase II clinical trials and the manufacturing of our commercial products.

We rely on outsourcing arrangements for some of our critical activities, including manufacturing, preclinical and clinical research, data collection and analysis, and electronic submission of regulatory filings. We may have limited control over third parties and we cannot guarantee that they will perform their obligations in an effective, competent and timely manner. Our reliance on third parties, including third-party CROs and CMO, entails risks including, but not limited to:

- Non-compliance by third parties with regulatory and quality control standards;
- Sanctions imposed by regulatory authorities if compounds supplied or manufactured by a third party supplier or manufacturer fail to comply with applicable regulatory standards;
- Possible breach of the agreements by the CROs or CMOs because of factors beyond our control, insolvency or other financial difficulties of any of these third parties, labor unrest, natural disasters or other factors adversely affecting their ability to conduct their business; and
- Termination or non-renewal of an agreement by a third party, at a time that is inconvenient for us, for reasons not entirely under our control.

We do not own or operate manufacturing facilities for the production of any of our products or product candidates beyond Phase II clinical trials, nor do we have plans in the foreseeable future to develop our own manufacturing operations to support Phase III clinical trials or commercial production. We currently depend on third-party CMOs for all of our required raw materials and drug substances for our preclinical research and

clinical trials. For Oxtellar XR and Trokendi XR, we currently rely on single source suppliers for raw materials, including API, and rely on third-party suppliers and manufacturers for the production and packaging final commercial products. If any of these vendors are unable to perform their obligations to us, including due to violations of the FDA's requirements, our ability to meet regulatory requirements, projected timelines, necessary quality standards for our development or commercialization products would be adversely affected. Further, if we were required to change vendors, it could result in substantial delays in our regulatory approval

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efforts and significantly increase our costs. Accordingly, the loss of any of our current or future third-party manufacturers or suppliers could have a material adverse effect on our business, results of operations, financial condition and business prospects.

If other versions of extended or controlled release oxcarbazepine or topiramate are approved and successfully commercialized, our business could be materially harmed.

Third parties have and may receive approval to manufacture and market their own versions of extended release oxcarbazepine or topiramate AEDs in the U.S. For example, Upsher-Smith launched Qudexy XR (extended release topiramate) and a branded generic version of Qudexy XR. Upsher Smith also entered into settlement with a generic company to launch a generic to Qudexy XR in 2020, and with another generic company to enter the market at a date that is unknown to us. Such generics could adversely impact the sales or prescriptions for Trokendi XR or result in an earlier entry of generics to Trokendi XR. In addition, since Trokendi XR was not granted marketing exclusivity by the FDA, we may not be able to prevent the submission or approval of another Full NDA for a competitor's extended or controlled release topiramate product candidate. However, we do have the right to defend our products against third parties who may infringe or are infringing our patents.

In addition, we are aware of companies who are marketing modified-release oxcarbazepine products outside of the U.S., such as Apydan, which was developed by Desitin Arzneimittel GmbH and requires twice-daily administration. If companies with modified-release oxcarbazepine products outside of the U.S. pursue or obtain approval of their products within the U.S., such competing products may limit the potential success of Oxtellar XR in the U.S., and our business and growth prospects could be materially impaired. Accordingly, if any third party is successful in obtaining approval to manufacture and market its own version of extended release oxcarbazepine or topiramate in the U.S., we may not be able to prospectively realize revenues from Oxtellar XR or Trokendi XR.

If we do not obtain marketing exclusivity for our product candidates, our business may suffer.

Under the Hatch-Waxman Amendments, three years of marketing exclusivity may be granted for the approval of new and sNDAs, including Section 505(b)(2) applications, for, among other things, new indications, dosage forms, routes of administration, strengths or for a new use, of an existing drug. If the clinical investigations that were conducted or sponsored by the applicant are determined by the FDA to be essential to the approval of the application, the FDA may grant exclusivity for the product, sometimes referred to as clinical investigation exclusivity, which prevents the FDA from approving an application under Section 505(b)(2) for the same conditions of use associated with the new clinical investigations before the expiration of three years from the date of approval. Such exclusivity, however, would not prevent the approval of another application if the applicant submits a Full NDA and has conducted its own adequate, well-controlled clinical trials demonstrating safety and efficacy, nor would it prevent approval of a generic product or Section 505(b)(2) product that did not incorporate the exclusivity-protected changes of the approved drug product.

Under the Hatch-Waxman Amendments, newly-approved drugs and indications may also benefit from a statutory period of non-patent marketing exclusivity. The Hatch-Waxman Amendments provide five-year marketing exclusivity to the first applicant to gain approval of an NDA for an NCE, meaning that the FDA has not previously approved any other drug containing the same API, or active moiety, which is the molecule responsible for the action of the drug substance. Although protection under the Hatch-Waxman Amendments will not prevent the submission or approval of another Full NDA, such an NDA applicant would be required to conduct its own preclinical and adequate, well-controlled clinical trials to demonstrate safety and effectiveness.

While the FDA granted a three year marketing exclusivity period for Oxtellar XR, it did not grant a similar marketing exclusivity period for Trokendi XR. If we are unable to obtain marketing exclusivity

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for our subsequent product candidates, then our competitors may obtain approval for competing products more easily than if we had such marketing exclusivity. Our future revenues could be reduced, possibly materially.

We may not obtain or maintain the benefits associated with orphan drug designation, including market exclusivity.

Regulatory authorities in the United States may designate drugs for relatively small patient populations as orphan drugs. The FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition that affects fewer than 200,000 individuals annually in the U.S.

In the U.S., orphan drug designation entitles a party to financial incentives, such as opportunities for grant funding towards clinical trial costs, tax credits for certain research and user fee waivers under certain circumstances. In addition, if a drug receives the first FDA approval for the drug and indication for which it has orphan drug designation, the drug is entitled to seven years of market exclusivity, which means the FDA may not approve any other application for the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the drug with orphan drug exclusivity.

Although we have been granted FDA orphan drug designation for SPN-817 for the treatment of Dravet Syndrome, and intend to continue to expand our designation for these uses where applicable, we may not receive the benefits associated with orphan drug designation. This may result from a failure to maintain orphan drug status or may result from a competing product reaching the market that has an orphan designation for the same disease indication. Under U.S. rules for orphan drugs, if such a competing product reaches the market before ours does, the competing product could potentially obtain a scope of market exclusivity that limits or precludes our product from being sold in the U.S. for seven years. Even if we obtain exclusivity, the FDA could subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Also, a competitor may receive approval of different products for the same indication for which our orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity.

In addition, in August 2017, the FDA Reauthorization Act of 2017 (FDARA) was enacted. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act, including the FDARA amendment, its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

We face significant competition in attracting and retaining talented employees. Further, managing succession for, and retention of, key executives is critical to our success, and our failure to do so could have an adverse impact on our future performance.

We may not be able to attract or motivate qualified management, scientific and clinical personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses. Our industry has experienced a high rate of turnover of management personnel in recent years. If we are not able to attract and motivate necessary personnel to accomplish our business objectives, we may experience constraints that may significantly impede the achievement of our objectives.

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Effective succession planning is also important to our long-term success. Failure to ensure effective transfer of knowledge and smooth transitions involving key employees and members of our management team could hinder our strategic planning and execution. In addition, our failure to adequately plan for succession of senior management and other key management roles or the failure of key employees to successfully transition into new roles could have a material adverse effect on our business and results of operations.

We are highly dependent on the development, regulatory, commercial and financial expertise of our management, particularly Jack A. Khattar, our President and Chief Executive Officer. Mr. Khattar has an employment agreement and other members of the senior management team have executive retention agreements, but these agreements do not guarantee the services of these executives will continue to be available to us. If we lose key members of our management team, we may not be able to find suitable replacements in a timely fashion, if at all. We cannot be certain that future management transitions will not disrupt our operations or generate concern among employees and those with whom we do business.

In addition to competition for personnel, our corporate offices are located in the greater Washington D.C. metropolitan area, an area that is characterized by a high cost of living. As such, we could have difficulty attracting experienced personnel to our Company and may be required to expend significant financial resources in our employee recruitment efforts.

If our competitors develop or market alternatives for treatment of our target indications, our commercial opportunities will be reduced or eliminated.

The pharmaceutical industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary therapeutics. We face competition from a number of sources, some of which may target the same indications as our products and product candidates, including large pharmaceutical companies, smaller pharmaceutical companies, biotechnology companies, academic institutions, government agencies and private and public research institutions. The availability of new products or approval for new indications for existing products may limit the demand for and the price we are able to charge for any of our products. We may be unable to differentiate our products from competitive offerings. In addition to competition with our currently marketed products, we anticipate that we will face intense competition when our pipeline product candidates are approved by regulatory authorities and we begin the commercialization process for these products.

There are currently no marketed products and no known products in development for the treatment of IA in patients with ADHD, autism or PTSD. However, the off-label use of risperidone (Risperdal) and aripiprazole (Abilify) to treat these conditions is common. These products are approved for irritability in autism which, as a result, may influence use of products to treat IA in patients with ADHD.

In addition, we are aware of several companies that have various product candidates under development for ADHD which may compete with our SPN-812 product candidate. Such companies include Sunovion, Ironshore/Highland and Otsuka.

Further new developments, including the development of other drug technologies, may render our products or product candidates obsolete or noncompetitive. As a result, our products and product candidates may become obsolete before we recover expenses incurred in connection with their development or realize revenues from their commercialization. Further, many competitors have substantially greater:

Capital resources;

Research and development resources and experience, including personnel and technology;

Drug development, clinical trial and regulatory resources and experience;

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Sales and marketing resources and experience;

Manufacturing and distribution resources and experience;

Name recognition; and

Resources, experience and expertise in prosecution and enforcement of intellectual property rights.

As a result of these factors, our competitors may obtain regulatory approval of their products more rapidly than we are able to or may obtain patent protection or other intellectual property rights that limit or block us from developing or commercializing our product candidates. Our competitors may also develop drugs that are more effective, more useful, better tolerated, subject to fewer or less severe side effects, more widely prescribed or accepted or less costly than ours and may also be more successful than us in manufacturing and marketing their products. If we are unable to compete effectively with the products of our competitors or if such competitors are successful in developing products that compete with any of our approved product candidates, our business, results of operations, financial condition and prospects may be materially and adversely affected. Mergers and acquisitions in the pharmaceutical industry may result in even more resources being concentrated at competitors. Competition may increase further as a result of advances made in the commercial applicability of technologies and greater availability of capital for investment.

Our products and our product candidates may be subject to restrictions or withdrawal from the market. We may be subject to penalties if we fail to comply with regulatory requirements.

Even though U.S. regulatory approval has been obtained for Trokendi XR and Oxtellar XR, the FDA may still impose significant restrictions on their indicated uses or marketing or impose ongoing requirements for costly post-approval studies. For example, both Trokendi XR and Oxtellar XR were approved on the basis of post-approval commitments, including development of additional age-appropriate formulations of the drugs and conduct of post-approval clinical studies in accordance with certain timelines laid out in the approval letters. Although we have made significant efforts, in certain cases we have been unable to meet these timelines. The post-approval commitments required the creation of new drug product formulations, which we have not been able to accomplish. To date, the only consequence of our failure to meet our PREA commitment deadlines has been a notation on FDA websites devoted to making the status of PREA publicly known.

We are also required to conduct an additional post-approval study with respect to Trokendi XR for the treatment of prophylaxis of migraine. If we do not meet our post-marketing commitments and are unable to show good cause for our inability to adhere to the timetables laid out in the approval letters, the FDA could take enforcement action against us, including withdrawal of approval. While we believe that we can show good cause for our inability to meet the timelines for our post-approval study requirements, the FDA may disagree.

Our product candidates would also be, and our approved product and our collaborators' approved products are subject to ongoing FDA requirements governing the labeling, packaging, storage, advertising, promotion, recordkeeping and submission of safety and other information. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with current good manufacturing practice (cGMP) regulations. If we, our collaborators or a regulatory authority discovers previously unknown problems with a product, including side effects that are unanticipated in severity or frequency, or problems with the facility where the product is manufactured, a regulatory authority may impose restrictions on that product or the manufacturer, including requiring withdrawal of the product from the market or suspension of manufacturing.

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If we or our collaborators, or our or our collaborators' approved products or product candidates, or the manufacturing facilities for our or our collaborators' approved products or product candidates fail to comply with applicable regulatory requirements, a regulatory authority may:

- Issue warning letters or untitled letters;
- Impose civil or criminal penalties;
- Suspend regulatory approval;
- Suspend any ongoing bioequivalence and/or clinical trials;
- Refuse to approve pending applications or supplements to applications filed by us;
- Impose restrictions on operations, including costly new manufacturing requirements, or suspension of production for a sustained period of time; or
- Seize or detain products or require us to initiate a product recall.

In addition, our product labeling, advertising, and promotion of our approved products are subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about prescription products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. Notwithstanding, physicians may nevertheless prescribe our products to their patients in a manner that is inconsistent with the approved label, which is known as "off label use". The FDA and other authorities actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have promoted off-label uses may be subject to significant sanctions. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. If we are found to have promoted off-label uses, we may be enjoined from such off-label promotion and become subject to significant liability, which would have an adverse effect on our reputation, business and revenues.

Further, the FDA's policies may change and additional government regulations may be enacted that could affect our products or prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

If we fail to produce our products and product candidates in the volumes that we require on a timely basis, or fail to comply with stringent regulations applicable to pharmaceutical drug manufacturers, we may face delays in the development and commercialization of our products and product candidates, or be required to withdraw products from the market.

We do not currently own or operate manufacturing facilities for the production of any of our products or for the commercial production of our product candidates, nor do we have plans to develop our own manufacturing operations for commercial products in the foreseeable future. We currently depend on third-party CMOs for the supply of the APIs for our products and product candidates, including drug substance for our preclinical research and clinical trials. For Oxtellar XR and Trokendi XR, we currently rely on single source suppliers for raw materials, including API, as well as single source suppliers to produce and package final dosage forms. Any future curtailment in the availability of raw materials could result in production or other delays with consequent adverse business effects. In addition, because regulatory authorities must generally approve raw material sources for pharmaceutical products, changes in raw material suppliers may result in production delays or higher raw material costs.

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The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Pharmaceutical companies often encounter difficulties in manufacturing, particularly in scaling up production of their products. These problems include manufacturing difficulties relating to production costs and yields, quality control, stability of the product and quality assurance testing and shortages of qualified personnel, as well as compliance with federal, state and foreign regulations. If we are unable to demonstrate stability in accordance with commercial requirements, or if our manufacturers were to encounter difficulties or otherwise fail to comply with their obligations to us, our ability to maintain or obtain FDA approval and to market our products and product candidates, respectively, would be jeopardized. In addition, any delay or interruption in producing clinical trial supplies could delay or prohibit the completion of our clinical trials, increase the costs associated with conducting our clinical trials and, depending upon the period of delay, require us to commence new trials at significant additional expense, or to terminate a trial.

Manufacturers of pharmaceutical products need to comply with cGMP requirements and other requirements as enforced by the FDA, including electronic tracking and submission. These requirements include quality control, quality assurance and the maintenance of records and documentation. Manufacturers of our products and product candidates may be unable to comply with these cGMP requirements and with other FDA and foreign regulatory requirements. A failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall, or withdrawal of product approval. If the safety of any of our products or product candidates is compromised due to failure to adhere to applicable laws or for other reasons, we may not be able to obtain regulatory approval for such product candidate or successfully commercialize such products, and we may be held liable for any injuries sustained as a result. Any of these factors could cause a delay in clinical development, regulatory submissions, approvals or commercialization of our product candidates, entail higher costs or result in our being unable to effectively commercialize our product candidates. Furthermore, if we fail to obtain the required commercial quantities on a timely basis from our suppliers and at commercially reasonable prices, we may be unable to meet demand for our approved products, and consequently lose potential revenues.

We depend on wholesalers and distributors for retail distribution of Oxtellar XR and Trokendi XR. If we lose any of our significant wholesalers or distributors, our business could be harmed.

The majority of our sales of Oxtellar XR and Trokendi XR are to wholesalers and distributors who, in turn, sell the products to pharmacies, hospitals and other customers. For the year ended December 31, 2018, three wholesale pharmaceutical distributors, AmerisourceBergen Drug Corporation, Cardinal Health, Inc. and McKesson Corporation, individually accounted for more than 30% of our total revenue in 2018, and collectively accounted for 98% of our total revenue in 2018. The loss by us of any of these wholesale pharmaceutical distributors' accounts or a material reduction in their purchases could have a material adverse effect on our business, results of operations, financial condition and prospects.

In addition, these wholesale customers comprise a significant part of the distribution network for pharmaceutical products in the U.S. This distribution network has undergone, and may continue to undergo, significant consolidation marked by mergers and acquisitions. As a result, a small number of large wholesale distributors control a significant share of the market. Consolidation of drug wholesalers has increased, and, as a result, may continue to increase competitive and pricing pressures on pharmaceutical products. We cannot assure you that we can manage these pricing pressures or that wholesaler purchases will not fluctuate unexpectedly from period to period.

Our sales of Oxtellar XR and Trokendi XR can be greatly affected by the inventory levels our respective wholesalers carry. We monitor wholesaler inventory of Oxtellar XR and Trokendi XR using a

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combination of methods. Pursuant to distribution service agreements with our three largest wholesale customers, we receive inventory level reports. For other wholesalers where we do not receive inventory level reports, our estimates of wholesaler inventories may differ significantly from actual inventory levels. Significant differences between actual and estimated inventory levels may result in excessive production (requiring us to hold substantial quantities of unsold inventory), inadequate supplies of products in distribution channels, and/or insufficient product available at the retail level. These changes may cause our revenues to fluctuate significantly from quarter to quarter, and in some cases may cause our operating results for a particular quarter to be below our expectations or the expectations of securities analysts or investors.

In addition, at times, wholesaler purchases may exceed customer demand, resulting in reduced wholesaler purchases in later quarters, which may cause substantial fluctuations in our results of operations from period to period. If our financial results are below expectations for a particular period, the market price of our common stock may drop significantly.

If the FDA or other applicable regulatory authorities approve generic products that compete with any of our products or product candidates, the sales of those products or product candidates would be adversely affected.

Once an NDA, including a Section 505(b)(2) application, is approved, the product covered thereby becomes a "listed drug" which can be cited by potential competitors in support of approval of an ANDA. FDCA, FDA regulations and other applicable regulations and policies provide incentives to manufacturers to create modified, non-infringing versions of a drug to facilitate the approval of an ANDA or other application for generic substitutes. These manufacturers might only be required to conduct a relatively inexpensive study to show that their product has the same active ingredient(s), dosage form, strength, route of administration, and conditions of use or labeling, as our product or product candidate and that the generic product is bioequivalent to our product. Bioequivalence implies that a product is absorbed in the body at the same rate and to the same extent as our product or product candidate. These generic equivalents, which must meet the same quality standards as branded pharmaceuticals, would be significantly less costly than ours to bring to market. Companies that produce generic equivalents are generally able to offer their products at significantly lower prices. Thus, regardless of the regulatory approval pathway, after the introduction of a generic competitor, a significant percentage of the sales of any branded product are typically lost to the generic product, through both price and volume erosion. Accordingly, competition from generic equivalents would materially, permanently and adversely impact our revenues, profitability and cash flows from those products and substantially limit our ability to obtain a return on the investments we have made in our products and product candidates. In particular, as disclosed in Part I, Item 3 *Legal Proceedings* of this Annual Report on Form 10-K, we had received Paragraph IV Notice Letters against our Oxtellar XR Orange Book patents from Twi Pharma. In August 2017, the U.S. District Court ruled in our favor against TWi concerning our Oxtellar XR patents. TWi filed a Notice of Appeal to the United States Court of Appeals for the Federal Circuit. On September 6, 2018, the Court of Appeals affirmed the District Court's Final Judgement and issued a mandate on October 16, 2018.

We intend to rely on third-party collaborators to market and commercialize our products and product candidates outside the U.S., who may fail to effectively commercialize our products and product candidates.

Outside the U.S., we utilize strategic partners where appropriate to assist in the commercialization of our products and product candidates. We currently possess limited resources and may not be successful in establishing collaborations or licensing arrangements on acceptable terms, if at all. We also face competition in our search for collaborators and licensing partners. By entering into strategic collaborations or similar arrangements, we will rely on third parties to financially support their local operations, including that required for development, commercialization, sales, marketing and regulatory activities as well as expertise in each of those subject areas. Our collaborators may fail to develop or

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effectively commercialize our products or product candidates because they cannot obtain the necessary regulatory approvals, they lack adequate financial or other resources or they decide to focus on other initiatives. Any failure of our third-party collaborators to successfully market and commercialize our products or product candidates outside the U.S. would diminish our revenues and harm our results of operations.

Limitations on our patent rights relating to our products and product candidates may limit our ability to prevent third parties from competing against us.

To a significant degree, our success will depend on our ability to obtain and maintain patent protection for our proprietary technologies and our products and product candidates, preserve our trade secrets, prevent third parties from infringing upon our proprietary rights and operate without infringing upon the proprietary rights of others. To that end, we seek patent protection in the U.S. and internationally for our products and product candidates. Our policy is to actively seek to protect our proprietary position by, among other things, filing patent applications in the U.S. and abroad (including Europe, Canada and certain other countries when appropriate) relating to proprietary technologies that are important to the development of our business.

The strength of patents in the pharmaceutical industry involves complex legal and scientific questions and can have uncertain results. Patent applications in the U.S. and most other countries are confidential for a period of time until they are published, and publication of discoveries in scientific or patent literature typically lags actual discoveries by several months or more. As a result, we cannot be certain that we were the first to conceive inventions covered by our patents and pending patent applications or that we were the first to file patent applications for such inventions. In addition, we cannot be certain that our patent applications will be granted, that any issued patents will adequately protect our intellectual property or that such patents will not be challenged, narrowed, invalidated or circumvented.

We also rely upon unpatented trade secrets, unpatented know-how and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with our employees and our collaborators and consultants. We also have agreements with our employees and selected consultants that obligate them to assign their inventions to us. It is possible that technology relevant to our business will be independently developed by a person that is not a party to such an agreement. Furthermore, if the employees and consultants that are parties to these agreements breach or violate the terms of these agreements, we may not have adequate remedies, and we could lose our trade secrets through such breaches or violations. Further, our trade secrets could otherwise become known or be independently discovered by our competitors. Any failure to adequately prevent disclosure of our trade secrets and other proprietary information could have a material, adverse impact on our business.

In addition, the laws of certain foreign countries do not protect proprietary rights to the same extent or in the same manner as the U.S., and therefore we may encounter problems in protecting and defending our intellectual property in certain foreign jurisdictions.

If we are sued for infringing intellectual property rights of third parties, it could be costly and time consuming to defend such a suit. An unfavorable outcome in that litigation could have a material adverse effect on our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our approved products and our product candidates and to use our proprietary technologies without infringing the proprietary rights of third parties. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we and our collaborators are developing product candidates. As the pharmaceutical

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industry expands and more patents are issued, the risk increases that our collaborators' approved products or our product candidates may give rise to claims of infringement of the patent rights of others. There may be issued patents of third parties of which we are currently unaware that may be infringed by our collaborators' approved products or Oxtellar XR or Trokendi XR, which could prevent us from being able to maximize revenue generated by our products or our product candidates. Because patent applications can take many years to issue, there currently may be pending patent applications which may later result in issued patents that our collaborators' approved products, our products, or our product candidates may infringe.

We may be exposed to, or threatened with, future litigation by third parties alleging that our collaborators' approved products or our products or product candidates infringe their intellectual property rights. If one of our collaborators' approved products, our products or our product candidates is found to infringe the intellectual property rights of a third party, we or our collaborators could be enjoined by a court and required to pay damages. We could be unable to commercialize the applicable approved products or product candidates unless we obtain a license to the patent. A license may not be available to us on acceptable terms, if at all. In addition, during litigation, the patent holder could obtain a preliminary injunction or other equitable relief which could prohibit us from making, using or selling our approved products prior to a trial. Such a trial may not occur for several years.

There is a substantial amount of litigation involving patent and other intellectual property rights in the pharmaceutical industry generally. If a third party claims that we or our collaborators infringe its intellectual property rights, we may face a number of issues, including, but not limited to:

- Infringement and other intellectual property claims which, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business;

- Substantial damages for infringement, which we may have to pay if a court decides that the product at issue infringes on or violates the third party's rights. If the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees;

- Court rulings prohibiting us from selling our products or product candidates unless the third party licenses its rights to us, which it is not required to do;

- If a license is available from a third party, we may have to pay substantial royalties, fees or grant cross-licenses to our intellectual property rights; and

- Redesigning our products or product candidates so they do not infringe, which may not be possible or may require substantial monetary expenditures and time.

We depend on collaborators to work with us to develop, manufacture and commercialize their and our products and product candidates.

We have a license agreement with United Therapeutics Corporation to use one of our proprietary technologies for an oral formulation of treprostinil diethanolamine, or treprostinil, for the treatment of pulmonary arterial hypertension, as well as for other indications. United Therapeutics Corporation launched Orenitram (treprostinil) in 2014, which triggered a milestone payment to us of $2.0 million. In the third quarter of 2014, we received a cash payment of $30.0 million as a result of HealthCare Royalty Partners III, L.P.'s (HC Royalty) purchase of certain of our rights under our license agreement with United Therapeutics Corporation related to the commercialization of Orenitram. We will retain full ownership of the royalty rights if/when a certain cumulative threshold payment to HC Royalty is reached. We are entitled to receive milestones and royalties for use of this formulation in other indications. If we materially breach any of our obligations under the license agreement, we could lose the right to receive any future royalty payments thereunder, which could be financially significant to us.

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Our future collaboration agreements may have the effect of limiting the areas of research and development that we may pursue, either alone or in collaboration with third parties. Much of the potential revenues from these future collaborations may consist of contingent payments, such as payments for achieving development milestones and royalties payable on sales of developed products. The milestone and royalty revenues that we may receive under these collaborations will depend upon our collaborators' ability to successfully develop, introduce, market and sell new products. Future collaboration partners may fail to develop or effectively commercialize products using our products, product candidates or technologies because they, among other things, may:

Change the focus of their development and commercialization efforts or may have insufficient resources to effectively develop our product candidates.

Pharmaceutical and biotechnology companies historically have re-evaluated their development and commercialization priorities following mergers and consolidations, which have been common in recent years. The ability of some of our product candidates to reach their potential could be limited if our future collaborators decrease or fail to increase development or commercialization efforts related to those product candidates;

Decide not to devote the necessary resources due to internal constraints, such as limited personnel with the requisite scientific expertise, limited cash resources, or the belief that other internal drug development programs may have a higher likelihood of obtaining marketing approval or may potentially generate a greater return on investment;

Develop and commercialize, either alone or with others, drugs that are similar to or competitive with the product candidates that are the subject of their collaboration with us;

Not have necessary and sufficient resources to carry the product candidate through clinical development, marketing approval and commercialization;

Fail to comply with applicable regulatory requirements;

Be unable to obtain the necessary marketing approvals; or

Breach or terminate their arrangement with us.

If collaboration partners fail to develop or fail to effectively commercialize our products for any of these reasons, we may not be able to replace the collaboration partner with another partner to develop and commercialize the product under the terms of the collaboration, if at all. Further, even if we are able to replace the collaboration partner, we may not be able to do so on commercially favorable terms. As a result, the development and commercialization of the affected product or product candidate could be delayed, curtailed or terminated because we may not have sufficient financial resources or capabilities to continue development and commercialization of the product candidate on our own.

We have in-licensed or acquired a portion of our intellectual property necessary to develop certain of our product candidates. If we fail to comply with our obligations under any of these arrangements, we could lose such licenses or intellectual property rights.

We are a party to and rely on several arrangements with third parties which give us rights to IP that are necessary for the development of certain of our product candidates. In addition, we may enter into similar arrangements in the future for other product candidates. Our current arrangements impose various development, financial and other obligations on us. If we materially breach these obligations or if third parties fail to adequately perform their respective obligations, these exclusive arrangements could be terminated, which would result in our inability to develop, manufacture, market and sell products that are covered by such IP.

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Even if our product candidates receive regulatory approval in the U.S., we or our collaborators may not receive approval to commercialize our product candidates outside of the U.S.

To market any products outside of the U.S., we must establish and comply with numerous and varying regulatory requirements of other jurisdictions regarding safety and efficacy. Approval procedures vary among jurisdictions and can involve product testing and administrative review periods different from, and greater than those in the U.S. The time required to obtain approval in other jurisdictions might differ from that required to obtain FDA approval. The regulatory approval process in other jurisdictions may include all of the risks detailed above regarding FDA approval in the U.S. as well as other risks. For example, legislation analogous to Section 505(b)(2) of the FDCA in the U.S., which relates to the ability of an NDA applicant to use published data not developed by such applicant, may not exist in other countries. In territories where data are not freely available, we may not have the ability to commercialize our products without negotiating rights from third parties to refer to their clinical data in our regulatory applications, which could require the expenditure of significant additional funds and time.

In addition, regulatory approval in one jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory processes in others. Failure to obtain regulatory approvals in