

SUPERNUS PHARMACEUTICALS INC
Form 10-K
March 15, 2013

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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, 2012

COMMISSION FILE NUMBER: 0-50440

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

(State or other jurisdiction of
incorporation or organization)

1550 East Gude Drive, Rockville, MD

(Address of Principal
Executive Offices)

(301) 838-2500

(Registrant's telephone number,
including area code)

20-2590184

(I.R.S. Employer
Identification Number)

20850

(zip code)

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

TITLE OF EACH CLASS:

Common Stock, \$0.001 Par Value

NAME OF EACH EXCHANGE ON WHICH REGISTERED:

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 o No ý

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

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subject to such filing requirements for the past 90 days. Yes No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 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.

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

Large accelerated
filer

Accelerated
filer

Non-accelerated filer
(Do not check if a
smaller reporting
company)

Smaller reporting
company

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

As of June 30, 2012, 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 \$19,554,538.

The number of shares of the registrant's common stock outstanding as of February 28, 2013 was 30,892,070.

DOCUMENTS INCORPORATED BY REFERENCE

Certain portions of the registrant's definitive Proxy Statement for its 2013 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 2012 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, 2012

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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®," "Microtrol®," "Solutrol®," "ProScreen®," "OptiScreen®," "ProPhile®," "Trokendi XR ," "Oxtellar XR ," and the registered Supernus Pharmaceuticals logo.

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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 "Business", "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere. 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

We are a specialty pharmaceutical company focused on developing and commercializing products for the treatment of central nervous system, or CNS, diseases. Our extensive expertise in product development has been built over the past 20 years: initially as a standalone development organization, then as a U.S. subsidiary of Shire plc and, upon our acquisition of substantially all the assets of Shire Laboratories Inc. in late 2005, as Supernus Pharmaceuticals. We launched Oxtellar XR (extended release oxcarbazepine), our first epilepsy product, in the first quarter of 2013 and anticipate the launch of a second epilepsy product, Trokendi XR (extended release topiramate), in the third quarter of 2013, and are developing multiple product candidates in psychiatry to address the large market opportunity in the treatment of attention deficit hyperactivity disorder, or ADHD, including ADHD patients with impulsive aggression. We intend to market our products in the United States through our own focused sales force targeting specialty physicians, which include neurologists and psychiatrists; and to seek strategic collaborations with other pharmaceutical companies to license our products outside the United States.

Our neurology portfolio consists of a marketed product and a tentatively approved product. On October 19, 2012, the Food and Drug Administration, or FDA, granted final approval of Oxtellar XR, as adjunctive therapy of partial seizures in adults and in children 6 years to 17 years of age. On November 15, 2012, the FDA granted Oxtellar XR a three year marketing exclusivity. The commercial launch of Oxtellar XR occurred during the first quarter of 2013. On June 25, 2012, the FDA granted tentative approval of Trokendi XR, as initial monotherapy in patients 10 years of age and older with partial onset or primary generalized tonic-clonic seizures, and as adjunctive therapy in patients 6 years of age and older with partial onset or primary generalized tonic-clonic seizures or with seizures associated with Lennox-Gastaut syndrome. The final approval for Trokendi XR may not be made effective until the expiration of the marketing exclusivity period that Topamax's new drug application, or NDA, (currently held by Johnson & Johnson, Inc.) has regarding safety information in a specific pediatric population. This marketing exclusivity expires on June 22, 2013. In early December, 2012, the Company submitted to the FDA a request for final approval as an amendment to the NDA including a safety data update, a new package insert and packaging configurations for Trokendi XR and was informed that should the FDA approve such amendment, it will most likely be in the form of a tentative approval because the review period of such amendment would be expected to conclude in the second quarter prior to the June 22, 2013 expiration of the pediatric exclusivity. The Company

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continues to expect getting the final approval and commercially launching Trokendi XR in the third quarter of 2013.

Our psychiatry product candidates include SPN-810 (molindone hydrochloride), which received positive topline results from its Phase IIb study for the treatment of impulsive aggression in ADHD patients, and SPN-812, which is also moving forward into later stage development, having successfully completed a Phase IIa trial as a novel non-stimulant treatment of ADHD.

We have several additional product candidates in various stages of development, including SPN-809 for which we submitted an investigational new drug application, or IND, in 2008. SPN-809 would represent a novel mechanism of action for the U.S. anti-depressant market. We believe our broad and diversified portfolio of product candidates provides us with multiple opportunities to achieve our goal of becoming a leading specialty pharmaceutical company focused on CNS diseases.

We use our proprietary technologies to enhance the therapeutic benefits of approved drugs through advanced extended release formulations. Oxtellar XR and Trokendi XR are novel oral once-daily extended release formulations of oxcarbazepine and topiramate, respectively, for the treatment of epilepsy. Oxtellar XR is the first and only extended release formulation of oxcarbazepine available in the U.S. We believe that Trokendi XR will be the first extended release formulation of topiramate for the treatment of epilepsy in the U.S. Immediate release formulations of oxcarbazepine and topiramate are available in generic form and are marketed by Novartis and Johnson & Johnson under the brand names of Trileptal and Topamax, respectively. According to IMS Health, peak sales of Trileptal and Topamax represented an estimated 8.1% and 25.8% of the total seizure disorder market in 2006 and 2008, respectively. We pursued a Section 505(b)(2) regulatory strategy for Oxtellar XR, which allowed us to rely on the existing data from the NDA of Trileptal. The formulations allowing once-per-day dosing of Oxtellar XR and Trokendi XR are designed to improve patient compliance and to possibly provide a better tolerability profile compared to the current immediate release anti-epileptic drugs, or AEDs, that must be taken multiple times per day to maintain therapeutic drug concentrations over the dosing interval. We believe there is a significant unmet need for extended release products, such as Oxtellar XR and Trokendi XR, for the treatment of epilepsy. Extended release products have been shown to improve compliance, increase seizure control, reduce side effects and improve tolerability(1) as compared to immediate release products.(2) We have two U.S. patents issued covering Oxtellar XR and two U.S. patents issued covering Trokendi XR.

(1) Miller, A.D., *Improved CNS tolerability following conversion from immediate-to extended-release carbamazepine*, published June 2004 in *Acta Neurologica Scandinavica*.

(2) Balzac, F., *Medication Noncompliance in Epilepsy*, published March 2006 in *Neurology Reviews*.

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Our development portfolio also includes treatments for new indications in diseases such as ADHD and its coexisting disorders. We are developing SPN-810, which completed a Phase IIb trial for which we received positive topline results in November 2012, as a novel treatment for impulsive aggression in patients with ADHD. Since we issued the topline results, we have been analyzing the full dataset and working on putting together a package that outlines our development plan including a proposed Phase III design to discuss in detail with the FDA later this year. If approved by the FDA, SPN-810 could be the first product available to address this serious, unmet medical need. SPN-810 is based on molindone hydrochloride, which was previously marketed in the United States as an anti-psychotic to treat schizophrenia under the trade name Moban. In addition, SPN-812, which completed a Phase IIa trial, is being developed as a novel non-stimulant treatment for ADHD. SPN-812 is a selective norepinephrine reuptake inhibitor that we believe could be more effective and have a better side effect profile than other non-stimulant treatments for ADHD. In addition, because the active ingredient of SPN-812 has demonstrated efficacy as an anti-depressant in Europe, this product candidate, if studied in that specific patient population and shown to be effective, may provide increased benefit to an estimated 40% of ADHD patients who suffer from depression.(3)

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

Product	Indication	Status
Oxtellar XR	Adjunctive therapy for epilepsy	Launched
Trokendi XR	Epilepsy	Tentative approval by FDA
SPN-810	Impulsive aggression in ADHD	Phase IIb completed
SPN-812	ADHD	Phase IIa completed
SPN-809	Depression	IND filed

We have a successful track record of developing novel products by applying proprietary technologies to known drugs to improve existing therapies and enable the treatment of new indications. We have a broad portfolio of drug development technologies consisting of six platforms that include the following: Microtrol (multiparticulate delivery platform), Solutrol (matrix delivery platform) and EnSoTrol (osmotic delivery system). Our proprietary technologies have been used in the following approved products: Carbatrol (carbamazepine), Adderall XR (mixed amphetamine salts), and Intuniv (guanfacine), marketed by Shire; Equetro (carbamazepine), marketed by Validus Pharmaceuticals Inc.; Sanctura XR (trospium chloride), marketed by Allergan, Inc.; and Oracea (doxycycline), marketed by Galderma Laboratories, L.P. We are continuing to expand our intellectual property portfolio to provide additional protection for our technologies and our product candidates. Throughout our 20 year history, we have continued our commitment to innovation with a focus for the past seven years on successfully developing our own product candidates in neurology and psychiatry.

Our Strategy

Our goal is to be a leading specialty pharmaceutical company developing and commercializing new medicines in neurology and psychiatry. Key elements of our strategy to achieve this goal are to:

Build in-house sales and marketing capabilities, focused on specialty markets in the United States, to promote Oxtellar XR and Trokendi XR. We have built our sales and marketing capabilities in the United States to launch Oxtellar XR and, assuming receipt of final approval from the FDA, Trokendi XR. Additionally, there are plans to further expand our sales and marketing capabilities later this year.

(3)

Biederman, J., *New Insights Into the Comorbidity Between ADHD and Major Depression in Adolescent and Young Adult Females*, published in April 2008 in *Journal of the American Academy of Child and Adolescent Psychiatry* and Report of CME Institute of Physicians Postgraduate Press, Inc., published in August 2008 in *Journal of Clinical Psychiatry*.

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Continue to advance our product candidates in our psychiatry portfolio, including SPN-810 and SPN-812. As part of our longer term strategy, we intend to further develop our product candidates in our psychiatry portfolio to enable further diversification of our pipeline and future growth. We completed a Phase IIb trial of SPN-810 for impulsive aggression in ADHD patients for which we received positive topline results in November 2012. We are planning to meet with the FDA to discuss next steps in the development program and the design and protocol for Phase III clinical trials.

Continue to develop differentiated products by applying our technologies to known drug compounds. We intend to continue our development activities on known drug compounds and compounds with established mechanisms of action thereby reducing the risks, costs and time typically associated with pharmaceutical product development. We intend to leverage our proprietary and in-licensed technologies, to expand our patent portfolio and further develop and protect our diverse pipeline of product candidates.

Establish strategic partnerships to accelerate and maximize the potential of our product candidates worldwide. We intend to continue to seek strategic collaborations with other pharmaceutical companies to commercialize our products outside the United States. We believe that we are an attractive collaborator for pharmaceutical companies due to our broad portfolio of proprietary technologies and our proven product development track record.

Leverage our management team's expertise to develop and commercialize our broad portfolio of product candidates. We intend to leverage the expertise of our executive management team in developing and commercializing innovative therapeutic products. 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 or, wherever appropriate, external collaborations.

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 or physical abilities. Epilepsy, which is typically diagnosed by a neurologist, is estimated to affect 50 million people worldwide⁽⁴⁾ and 2 million people in the United States.⁽⁵⁾ According to IMS Health, U.S. sales of AEDs were approximately \$4.0 billion in 2011. The annual cost of epilepsy to the healthcare system is estimated to be \$12.5 billion.⁽⁶⁾

(4) Bialer, M., *Key factors in the discovery and development of new antiepileptic drugs*, published January 2010 in *Nature*.

(5) U.S. Centers for Disease Control and Prevention, *Epilepsy Self-Management Tools* (citing DiLorio, C., *The Prevention Research Centers' Managing Epilepsy Well Network*, published September 2010 in *Epilepsy & Behavior*).

(6) Epilepsy Foundation, *Cost Study Shows Divide in Treatment Effects*, published April 2000.

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Epileptic seizures can cause a person to experience severe muscle jerking, to lose consciousness and fall, or to suffer from distorted vision, all potentially leading to physical injuries or hospitalization. Until reliable seizure control has been achieved, patients are forced to adjust their lifestyles to avoid activities that a seizure can significantly disrupt or render life threatening. A breakthrough seizure is a sudden, unexpected seizure experienced by a patient who previously had achieved reliable seizure control. Even when no physical injury occurs, breakthrough seizures often result in significant social, legal and developmental consequences for patients such as loss of driver's license, loss of employment, disruption of school attendance, academic underachievement, and disruption of social networks. In addition, a single breakthrough seizure can lead to permanent loss or reduction in overall seizure control. Data suggest that a significant proportion of patients who experience a breakthrough seizure have a lower chance of achieving reliable seizure control.(7) In certain cases, a single breakthrough seizure can develop into *status epilepticus*, a prolonged seizure or series of repeated seizures, and eventually result in brain damage or death. Data indicate that the risk of sudden unexpected death in epilepsy was 23 times higher in patients who had at least one breakthrough seizure compared to patients who had achieved seizure control.(8)

Current Treatment Options

Once a patient is diagnosed with epilepsy, the goal of the neurologist is to find the particular drug or combination of drugs, and appropriate dosing, that will lead the patient to reliable seizure control while minimizing side effects. There are currently over 15 approved AEDs marketed in the United States. Side effects play a major role in altering treatment in epilepsy as they can limit the usefulness of AEDs. AEDs are generally associated with the incidence of numerous side effects that can adversely impact the quality of life for patients with epilepsy. Such side effects may include dizziness, paresthesia, headaches, cognitive deficiencies such as memory loss and speech impediment, digestive problems, somnolence, double vision, gingival enlargement, nausea, weight gain, and fatigue. To address these side effects and help patients better tolerate their AEDs, neurologists typically initiate treatment with a single AED as monotherapy at a low dose and then increase the dose to a higher level until the patient reaches the most efficacious dose with an acceptable tolerance of side effects.

Many patients develop refractory epilepsy, which refers to inadequate control of seizures despite treatment, thereby requiring treatment with multiple AEDs. Patients taking more than one AED at a time are susceptible to side effects associated with each of the multiple drugs and with drug interactions. Despite the introduction of new AEDs in the past few years, drug therapy remains ineffective for seizure control in up to 30% of patients with epilepsy.(9) Many patients fail drug therapy either because the drugs do not control their seizures or because they cannot tolerate the side effects.

(7) Citizen Petition of UCB, Inc. to U.S. Food and Drug Administration, submitted October 3, 2006 (citing Schmidt, D., *Uncontrolled epilepsy following discontinuation of antiepileptic drugs in seizure-free patients: a review of current clinical experience*, published December 2005 in *Epilepsia*).

(8) Citizen Petition of UCB, Inc. to U.S. Food and Drug Administration, submitted October 3, 2006 (citing Tomson, T., *Sudden unexpected death in epilepsy: a review of incidence and risk factors*, published May 2005 in *Acta Neurologica Scandinavica*).

(9) World Health Organization, *Epilepsy: aetiology, epidemiology and prognosis*, Fact Sheet No. 165, revised February 2001.

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Dynamics of the Epilepsy Market

There are several important dynamics that play a major role in the treatment of epilepsy and that differentiate epilepsy from many other diseases:

Compliance is Critical to the Reduction in Breakthrough Seizures

Compliance with drug treatment regimens is critically important to achieving effective therapy for patients with epilepsy where the consequences of non-compliance can be life threatening. Patient non-compliance with AED therapy is a serious issue and remains one of the most common causes of breakthrough seizures. Not only is taking all prescribed doses critical for epileptic patients, but the timing of when patients take their prescribed doses is also important. Typically, non-compliance is caused by frequent or multiple dosing, serious side effects, or a lack of tolerability. A 2002 survey undertaken by neurologists in the United States found that, at least once per month, 71% of patients with epilepsy forgot to take their AED, and it was evident that the chances of a patient missing a dose increased with the number of tablets prescribed.(10) Of patients that missed a dose, 45% reported a breakthrough seizure. Patients taking a larger number of tablets/capsules further increased their odds of having a breakthrough seizure by 43% after a missed dose. Other studies also have shown reduced rates in breakthrough seizures as a result of improved compliance with AED treatment regimens. In addition, a non-compliant patient can cost the healthcare system approximately an additional \$16,300 per year when compared to a compliant patient.(11)

(10)

Cramer, J.A., *The relationship between poor medication compliance and seizures*, published August 2002 in *Epilepsy & Behavior*.

(11)

Faught, R.E., Weiner, J.R., Guérin, A. et al., *Impact of nonadherence to antiepileptic drugs on healthcare utilization and costs: Findings from RANSOM study*, published March 2009 *Epilepsia*; 50:501-9.

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Immediate Release Products Have Serious Side Effects and Lack of Tolerability

The FDA has recognized AEDs as being "critical dose drugs," or drugs in which a comparatively small difference in dose or concentration may lead to serious therapeutic failures and/or serious side effects. Immediate release formulations of AEDs necessitate frequent administration to maintain appropriate plasma concentrations. However, these immediate release formulations cause wide fluctuations of blood levels of the active drug during the day, with peak concentrations when the drug is released and potentially sub-therapeutic concentrations thereafter. At least one study has shown that complaints of side effects typically occur when blood levels exceed certain concentrations, particularly at high doses, and the risk of breakthrough seizures can occur when blood levels are below certain minimum effective levels, as indicated in the chart below.

**Simulated Plasma Concentration-Time Curve at Steady State of Immediate Release
Anti-Epileptic Drug Administered Over Two Days**

Source: Pellock, JM et al, *Epilepsy & Behavior* 5 (2004), 302

Generic Substitution Can Cause an Increase in Breakthrough Seizures

Patients today are most typically switched from branded drugs to generics, or from one generic drug to another, mainly to reduce cost. In most states, unless a physician explicitly writes "dispense as written" or "no substitution," pharmacists can switch a patient to a lower-cost generic drug without the consent of either the patient or the physician. Epilepsy patients are particularly vulnerable to changes in their drugs or formulations because slight variations in the blood concentrations of these drugs could lead to the occurrence of breakthrough seizures. Accordingly, despite existing regulatory criteria to ensure the bioequivalence of generic drugs, the "switch-back" rates of AEDs (that is, the frequency of an individual being returned to his or her previous branded product under a physician's guidance) is much higher than for many other drug products. For example, the rates of patients switching back from generics to branded drugs because of adverse events were found to be 20.8% to 44.1% for AEDs compared to 7.7% to 9.1% for non-AEDs.(12)

(12)

J. LeLorier, *Clinical consequences of generic substitution of lamotrigine for patients with epilepsy*, published October 2008 in

Neurology.

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A number of epilepsy advocacy groups such as the Epilepsy Foundation of America, the American Academy of Neurology, the Centers for Medicare and Medicaid Services and several regulatory agencies around the world, including the UK National Institute for Health and Clinical Excellence, or NICE, Sweden's Medical Products Agency, or MPA, and other European agencies, have all acknowledged that AED generic substitutions for non-therapeutic reasons can be harmful and should either be limited or not permitted, and have issued guidelines, recommendations or taken affirmative steps to limit such substitutions. Additionally, approximately 88% of physicians indicate that they are concerned with the increase in breakthrough seizures resulting from switching from branded drugs to generics.⁽¹³⁾ While we are not aware of any well-controlled studies conducted to establish unequivocal scientific evidence that generic substitutions cause increased incidence of breakthrough seizures, the FDA is currently considering stricter standards of bioequivalence for generics and its Pharmaceutical Science and Clinical Pharmacology Advisory Committee voted 11-2 that the current bioequivalence standards are insufficient for critical dose drugs such as AEDs.

Physicians are Reluctant to Switch to New Chemical Entities

In the epilepsy market, new chemical entities, or NCEs, generally lack the same appeal that would typically be associated with a new drug for other indications. Based on IMS Health prescription data from 1994 to 2005 for NCE launches for seizure disorders, such NCEs, on average, experienced slow market penetration, characterized by a 0.58% to 1.1% market share point gain on an annual basis. We believe this is because physicians are often reluctant to change a stable patient's existing therapy and risk a breakthrough seizure in the patient. Despite the introduction of several NCEs over the past decade, a significant number of epileptic patients continue to lack reliable seizure control. Many NCEs continue to be associated with several side effects. Therefore, many older and existing drugs continue to be prescribed and their prescription levels have either been maintained since their peak or declined very slowly.

Benefits of Extended Release Products in the Epilepsy Market

Extended Release Products Improve Compliance and Reduce Breakthrough Seizures

Achieving reliable seizure control for patients and avoiding the serious health and life dangers that can be associated with breakthrough seizures depends on patients being compliant and diligent in taking their medications. Frequent and multiple dosing, side effects and lack of tolerability of the immediate release products can significantly contribute to patients forgetting doses or skipping them. Even taking a second or third dose later than the scheduled time may place a patient at an increased risk of a breakthrough seizure because the drug level in the patient's blood could drop below the minimum effective therapeutic level that prevents such seizures. We believe increased patient compliance can be achieved with extended release products that offer once-daily dosing, reduced side effects and improved tolerability. We believe physicians understand that the release profiles of extended release products can produce more consistent and steadier blood levels as compared to immediate release products, resulting in fewer side effects and better tolerability that further help patients to be compliant, have fewer breakthrough seizures and, correspondingly, enjoy a better quality of life.

Extended Release Products Reduce Side Effects and Improve Tolerability

When extended release formulations are used appropriately, drug levels remain within the patient's therapeutic zone, thereby reducing patient exposure to fluctuating drug levels, which may exacerbate side effects or induce breakthrough seizures. Because extended release formulations can reduce peak concentrations, it may also be possible to adjust doses upward to a more efficacious level without exacerbating side effects associated with peak concentrations. Extended release formulations can also

(13)

Dalia Buffery, MA, ABD, *Switching to Generics Antiepileptic Drugs: Growing Concerns*, published September 2008 in *American Health & Drug Benefits*.

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reduce the frequency and the extent of the troughs, or lower concentrations of the drug in the blood, thereby avoiding concentrations below the minimum effective concentrations that can increase the risk of breakthrough seizures.

Simulated Plasma Concentration-Time Curve at Steady State of Immediate Release and Extended Release Anti-Epileptic Drug Administered Over Two Days

Source: Pellock, JM et al, *Epilepsy & Behavior* 5 (2004), 302

The enhanced safety profile of extended release products as compared to similar immediate release products has been supported by several studies. For example, in a 2004 published trial conducted by physicians at Johns Hopkins, Carbatrol, an anti-epileptic extended release carbamazepine product that uses our Microtrol technology, and Tegretol XR, another extended release carbamazepine product, demonstrated better tolerability and side effect profiles than comparable immediate release products. The trial reported that 49% of patients had side effects during treatment with immediate release carbamazepine such as sedation, double-vision, confusion, ataxia, dizziness or poor coordination, whereas with extended release carbamazepine treatments, only 20% of patients reported these side effects.

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**Reduction in CNS Side Effects Following Conversion to Carbamazepine Extended Release
from Immediate Release Preparation**

Source: Miller AD et al., Acta Neurol. Scand 2004; 109: 374-377

Equally as important, the patients in the trial tolerated high doses of extended release carbamazepine significantly better than high doses of immediate release carbamazepine. Specifically, 63% of patients treated with 1200 mg or more per day of immediate release carbamazepine developed side effects, yet only 12% of patients experienced side effects while taking similar doses of extended release carbamazepine. The investigators surmised that the improved tolerability of extended release carbamazepine at high doses may provide a treatment option for patients previously discontinuing immediate release carbamazepine because of dose-limiting side effects.

Other products where reductions in side effects were reported by patients when switching from immediate release to extended release formulations include Depakote ER (divalproex sodium extended release) and Keppra XR (levetiracetam extended release).

Managed Care Does Not Limit Success of Extended Release Products

Given the serious nature of epilepsy and the key dynamics in the epilepsy market, we believe managed care plans acknowledge the important benefits of extended release AED products and, therefore, have not limited the success of such products even when lower cost generic immediate release products are available. For example, according to industry data, the recent commercial launches of extended release products Keppra XR and Lamictal XR have enjoyed acceptance rates by managed care plans that are similar to those of the corresponding immediate release products. Most managed care plans also acknowledge the position of several patient advocacy groups and the American Academy of Neurology regarding the risks of generic substitution of AEDs, including potential for breakthrough seizures. Although switching to a low-cost generic AED may initially offer some cost savings, we believe they also recognize that the risk and cost of one breakthrough seizure outweighs the potential savings from generics. For example, the healthcare costs associated with the treatment of patients who experience breakthrough seizures, which may run in excess of \$26,000 per patient on an annual basis, is significantly greater than any cost savings per patient that may be achieved through switching to a low-cost generic AED. According to a 2009 survey, the total healthcare costs for patients using branded

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topiramate products were approximately 20% lower than for patients using multiple generic topiramate products.(14)

Extended Release Products Perform Well in the Market

Extended release products have generally performed well in the epilepsy market, even in the face of immediate release generic products. Moreover, IMS Health prescription data for seizure disorder drugs from 1994 to 2005 shows that extended release products perform better than NCEs during the first five years of their commercial launch. Currently, there are five extended release AEDs on the market (Tegretol XR, Carbatrol, Depakote ER, Lamictal XR, Keppra XR), as reflected in the chart below, with Depakote ER gaining almost 40% of all divalproex prescriptions, including immediate release versions of Depakote and generic divalproex, in its fifth year after commercial launch. We believe that the modest conversion of the corresponding molecule prescriptions of the recent commercial launches of Keppra XR and Lamictal XR are due to limited promotional support behind both products.

**Comparison of Molecule Conversion of Extended Release Anti-Epilepsy Drugs
(measured as percentage of total prescriptions for each individual molecule)**

Source: IMS Health

Our Neurology Portfolio

We have developed a promising epilepsy product portfolio consisting of Oxtellar XR and Trokendi XR that utilize our proprietary technologies, Solutrol and Microtrol, respectively, each of which has been proven and validated through use in products that are currently on the market. Among them is Carbatrol, an AED that has been shown to reduce side effects compared to immediate release carbamazepine products. We believe that our 20 years of history and portfolio of technologies have enabled us to develop highly-customized product candidates that overcome challenges of the molecules' pharmacokinetic profiles. Our differentiated approach to product development and the strength of our technologies have allowed us to develop a once-daily formulation of oxcarbazepine with Oxtellar XR

(14)

Duh, M.S., *The risks and costs of multiple-generic substitution of topiramate*, published June 2009 in *Neurology*.

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where others have failed, and to develop Trokendi XR with what we believe to be a unique pharmacokinetic profile.

Oxtellar XR and Trokendi XR are novel extended release formulations of two well known and approved AEDs, oxcarbazepine and topiramate, respectively. Both formulations are designed to offer epilepsy patients effective therapy, reduced side effects and improved compliance with once-per-day dosing. We believe that by delivering more consistent and steady maintenance of blood level concentrations of oxcarbazepine and topiramate, respectively, Oxtellar XR and Trokendi XR can potentially reduce adverse side effects and improve tolerability of the drugs, which can improve compliance and enable patients to benefit from better seizure control and fewer breakthrough seizures as compared to similar immediate release products. Given that Oxtellar XR and Trokendi XR are based on different drug compounds and different mechanisms of action, they would target different market segments and patient populations within the epilepsy market.

The FDA approved our NDA for Oxtellar XR on October 19, 2012 as adjunctive therapy for partial seizures in adults and in children 6 years to 17 years of age and we launched the product on February 4, 2013. The FDA granted tentative approval of Trokendi XR on June 25, 2012, as initial monotherapy in patients 10 years of age and older with partial onset or primary generalized tonic-clonic seizures, and as adjunctive therapy in patients 6 years of age and older with similar seizures or with seizures associated with Lennox-Gastaut syndrome. The final approval for Trokendi XR may not be made effective until the expiration of the marketing exclusivity protection that Topamax has regarding safety information of topiramate in a specific pediatric population, which expires on June 22, 2013. We are not required to complete any additional clinical trials for Trokendi XR. In early December, 2012, the Company submitted to the FDA a request for final approval as an amendment to the NDA including a safety data update, a new package insert and packaging configurations for Trokendi XR and was informed that should the FDA approve such amendment, it will most likely be in the form of a tentative approval because the review period of such amendment would be expected to conclude in the second quarter prior to the June 22, 2013 expiration of the pediatric exclusivity. The Company continues to expect getting the final approval and commercially launching Trokendi XR in the third quarter of 2013. If we are successful in obtaining final FDA approval, we believe that Trokendi XR will be the first once-daily topiramate product approved for the monotherapy and adjunct therapy of epilepsy. We believe that Trokendi XR could, over time, capture a significant share of the topiramate prescriptions, consistent with the performance of similar extended release products that have been introduced in the U.S. epilepsy market during the last 15 years.

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Oxtellar XR (extended release oxcarbazepine)

Oxtellar XR is a novel oral once-daily extended release formulation of oxcarbazepine, which we launched on February 4, 2013. The product was approved by the FDA on October 19, 2012 as adjunctive therapy of partial seizures in adults and in children 6 years to 17 years of age and will have three years of marketing exclusivity. In addition, two U.S. patents have been issued covering Oxtellar XR. Oxtellar XR delivers oxcarbazepine, another effective AED, which is marketed by Novartis under the brand name Trileptal and is available in a generic form. Trileptal was initially developed and approved in the United States in 2000. Trileptal is indicated for monotherapy and adjunctive therapy of epilepsy. It reached peak worldwide sales of \$721 million in 2006, before generic products entered the U.S. market in October 2007.⁽¹⁵⁾ With approximately 3.4 million total oxcarbazepine prescriptions in 2011 and 3.5 million prescriptions in 2012, oxcarbazepine represents approximately 2.8% of total AED prescriptions, according to data from IMS Health. Oxcarbazepine is an active voltage-dependent sodium channel blocker that, despite its effectiveness in treating epilepsy, is associated with many side effects that tend to limit its use. The side effects associated with taking oxcarbazepine include, among others, dizziness, double vision, somnolence, nausea, fatigue and vomiting. Oxtellar XR has been designed to reduce side effects, resulting in improved patient compliance and tolerability.

With its novel pharmacokinetic profile that delivers lower peak plasma concentrations, slower rate of input and smoother and more consistent blood levels compared to immediate release products such as Trileptal, we believe Oxtellar XR has the potential of improving the tolerability of oxcarbazepine by reducing the side effects experienced by patients. This could enable more patients to effectively tolerate higher doses of oxcarbazepine, which would permit them to benefit from the resulting efficacy and greater seizure control that have been previously reported in patients at higher doses. In addition, Oxtellar XR once-per-day dosing is designed to improve patient compliance compared to the current immediate release products that are taken multiple times per day.

Oxtellar XR Development Program

We submitted an NDA for Oxtellar XR that was accepted for filing by the FDA in February 2012 and approved on October 19, 2012. The various clinical trials conducted on Oxtellar XR and that supported the NDA were designed to select the best extended release once-per-day formulation that delivers equivalent levels of oxcarbazepine compared to immediate release twice-per-day Trileptal, as well as to test the robustness and consistency of our technology in delivering the once-per-day formulation across a full range of product strengths. We also have scaled up our production of Oxtellar XR through our contract manufacturing organization, or CMO, at its commercial manufacturing facility, and will scale up commercial production of Trokendi XR in preparation for final FDA approval, if received.

In our pilot clinical trial in 32 healthy subjects, which took place in Canada, Oxtellar XR demonstrated a superior adverse event profile when compared to the immediate release oxcarbazepine therapy Trileptal. In this trial, a single center, open-label, randomized, two-way crossover, two-sequence trial, we compared multiple dose administration of Oxtellar XR tablets and Trileptal tablets in 32 healthy adult volunteers under fasting conditions. While the steady-state crossover comparison trial was designed to evaluate the steady-state bioavailability of the different formulations of oral oxcarbazepine at 1200 mg doses, the trial also assessed the safety and tolerability of repeat oral dosing of Oxtellar XR tablets in healthy subjects at 1200 mg in comparison to Trileptal.

(15) Based on sales data as reported in Novartis AG's Annual Report on Form 20-F for the fiscal year ended December 31, 2006 and in a media release issued by Novartis International AG on January 21, 2008.

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In this trial, the adverse events, or AEs, were observed in 30 healthy subjects using a total daily dose of 1200 mg of each of Trileptal and Oxtellar XR. There were 190 total AEs reported for Trileptal, while Oxtellar XR generated a total of only 120 AEs, a reduction of 37%. Of these, a total of 197 AEs were considered by the principal investigator to be possibly drug related: 131 for Trileptal and 66 for Oxtellar XR. More specifically, Trileptal demonstrated a 36.7% occurrence rate of dizziness as compared to Oxtellar XR which demonstrated a 0.0% occurrence rate in our trial. In other trials, Oxtellar XR demonstrated higher occurrence rates of dizziness. The results from these trials and the pilot clinical trial are preliminary and based on small populations.

In the pivotal Phase III trial for Trileptal, refractory patients had increasing reductions in seizures as dose levels increased, including 50% median reduction in seizures at the highest dose of 2400 mg. However, Trileptal is not without a host of side effects at the highest doses, which result in many subjects discontinuing treatment. Approximately 67% of subjects at the 2400 mg dose of Trileptal and 36% of subjects at the 1200 mg dose discontinued their participation in the trial because of the adverse events associated with the drug.

Epilepsy can be broadly characterized into partial and generalized seizures. Partial seizures occur in a specific location of the brain, affecting the physical or mental activity controlled by that particular area of the brain, whereas generalized seizures occur throughout both hemispheres of the brain at once. Partial seizures may be further subdivided into both simple and complex seizures. This refers to the effect of such a seizure on consciousness; simple seizures cause no interruption to consciousness (although they may cause sensory distortions or other sensations), whereas complex seizures interrupt consciousness to varying degrees.

The Phase III trial of Oxtellar XR was a multi-center, multiple-dose, randomized (1:1:1 ratio), double-blind, placebo-controlled, three-arm, parallel group trial in male and female subjects (18 to 65 years of age, inclusive) with refractory partial epilepsy on at least one and up to three concomitant AEDs. The trial was completed with 366 patients comprising the intent-to-treat, or ITT, population and 248 completing the study across 8 different countries in North America and Europe. Patients were randomized to one of three treatment groups, and took either Oxtellar XR (1200 mg/day or 2400 mg/day) or placebo.

The primary objective of the trial was to evaluate the efficacy of Oxtellar XR as an adjunctive therapy in the treatment of seizures of partial origin in adults with refractory epilepsy on at least one and up to three other AEDs. The secondary objectives were to primarily assess the safety and tolerability of adjunctive Oxtellar XR in the treatment of seizures of partial origin in subjects with refractory epilepsy on at least one and up to three other AEDs.

The primary endpoint was the median percentage change from baseline in partial seizure frequency per 28 days. Seizure frequency was assessed at baseline over 4-8 weeks. Patients had to have experienced a minimum of 3 seizures in a 28-day period to be included in the study. Drug titration to 1200 mg or 2400 mg occurred over 4 weeks using increments of 600 mg/week, and then was maintained between 12 and 13 weeks.

The median seizure reduction achieved in the study was 43% for Oxtellar XR 2400 mg/day with a p-value (p) of 0.003 versus placebo (123 patients), 38% for Oxtellar XR 1200 mg/day with p= 0.078 versus placebo (122 patients), and 29% for placebo (121 patients). In North America, the median reduction was 53% (35 patients) for Oxtellar XR 2400 mg/day with p=0.006 versus placebo, 35% (40 patients) for Oxtellar XR 1200 mg/day with p=0.022 versus placebo, and 13% for placebo (41 patients).

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Percent Median Seizure Reduction per 28 Days: All Countries

Percent Median Seizure Reduction per 28 Days: North America

Secondary endpoints included treatment response (i.e., how many responders had $\geq 50\%$ reduction in partial seizure frequency), and how many patients were seizure-free. At 2400 mg/day, Oxtellar XR provided significant treatment response ($p=0.018$) and seizure-free rates during treatment ($p=0.013$) and maintenance ($p=0.008$) periods versus placebo.

Table of Contents**Treatment Response and Seizure-Free Rates (ITT Population)**

	Oxtellar XR 1200 mg/day (n=122)	Oxtellar XR 2400 mg/day (n=123)	Placebo (n=121)
Treatment response			
n	109	111	117
Responder, n (%)	44 (36.1)	50 (40.7)	34 (28.1)
Non-responder, n (%)	65 (53.3)	61 (49.6)	83 (68.6)
<i>P</i> value versus placebo	0.075	0.018	
Seizure-free rates (treatment phase)			
Subjects with valid diary entry	109	111	117
Seizure free, n (%)	6 (4.9)	14 (11.4)	4 (3.3)
<i>P</i> value versus placebo	0.528	0.013	
Seizure-free rates (maintenance phase)			
Subjects with valid diary entry	97	88	109
Seizure free, n (%)	4 (3.3)	17 (13.8)	7 (5.8)
<i>P</i> value versus placebo	0.546	0.008	

Safety assessments were conducted throughout the study. AE rates were similar for patients receiving placebo and Oxtellar XR 1200 mg/day (55.4% and 56.6%, respectively); AE rates were slightly higher in patients receiving Oxtellar XR 2400 mg/day (69.1%). The most frequently reported AEs with Oxtellar XR were dizziness, somnolence, headache, nausea, double vision, and vomiting. Treatment-related AEs occurred in 58.5%, 43.4% and 38.8% of those on Oxtellar XR 2400 mg/day, Oxtellar XR 1200 mg/day, and placebo, respectively. Severe AEs occurred in 7.3%, 9.0% and 8.3% of those on Oxtellar XR 2400 mg/day, 1200 mg/day, and placebo, respectively. Severe treatment-related AEs occurred in 6.5%, 6.6% and 4.1% of those on Oxtellar XR 2400 mg/day, Oxtellar XR 1200 mg/day, and placebo, respectively. Serious AEs occurred in 8.1%, 5.7%, and 5.8% of those on Oxtellar XR 2400 mg/day, Oxtellar XR 1200 mg/day, and placebo, respectively. Treatment-related serious AEs occurred in 4.9%, 0% and 2.5% of those on Oxtellar XR 2400 mg/day, Oxtellar XR 1200 mg/day, and placebo, respectively. One death (resulting from ovarian cancer) occurred on placebo and no deaths occurred on Oxtellar XR therapy. AEs led to study discontinuation in 12.4% (n=15) of patients receiving placebo, 16.4% (n=20) of patients receiving Oxtellar XR 1200 mg/day, and 30.1% (n=37) of patients receiving Oxtellar XR 2400 mg/day.

In summary, Oxtellar XR 2400 mg/day significantly reduced partial seizure frequency from baseline versus placebo. Seizure frequency reduction with Oxtellar XR 1200 mg/day was greater than but did not separate from placebo. This finding may be explained by the high placebo response rate noted in some of the sites outside the U.S. in this study and is consistent with a general trend of higher placebo response rates observed in pivotal studies of other new AEDs. Although the 1200 mg/day dose did not reach statistical significance when compared to placebo, concentration response analyses revealed that the 1200 mg/day dose is effective and, therefore, was included in the Oxtellar XR approved label by the FDA as a recommended daily dose. Both Oxtellar XR doses were generally well tolerated with no new safety signals observed. The improved tolerability of Oxtellar XR, especially at doses up to 2400 mg/day, may translate to improved adherence and better patient outcomes.

Commercialization Strategy

Oxtellar XR is the only once-daily oxcarbazepine product indicated for the treatment of epilepsy in the U.S. as an adjunctive therapy and competes against the existing immediate release oxcarbazepine products on the market. We believe that Oxtellar XR could, over time, capture a significant share of the oxcarbazepine prescription market, consistent with the performance of similar extended release products that have been introduced in the U.S. epilepsy market over the past 15 years. In early 2013, to

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support the commercial launch of Oxtellar XR, which was granted three years of market exclusivity by the FDA, we built a small specialty sales force of approximately 75 representatives. These sales representatives are primarily targeting neurologists to promote the use of Oxtellar XR as adjunctive therapy of partial seizures in adults and in children 6 years to 17 years of age in the United States. We expanded our agreement with the CMO to provide for the production of commercial quantities of Oxtellar XR to fulfill expected demand through the commercial launch of the product.

Trokendi XR (extended release topiramate)

Trokendi XR is a novel oral once-daily extended release topiramate product for the treatment of epilepsy. The FDA issued a tentative approval of Trokendi XR in June 2012, as initial monotherapy in patients 10 years of age and older with partial onset or primary generalized tonic-clonic seizures, and as adjunctive therapy in patients 6 years of age and older with similar seizures or with seizures associated with Lennox-Gastaut syndrome. The final approval for Trokendi XR may not be made effective until the period of marketing exclusivity protection associated with safety information regarding a specific pediatric population, which expires on June 22, 2013. We are not required to complete any additional clinical trials for Trokendi XR. In early December, 2012, the Company submitted to the FDA a request for final approval as an amendment to the NDA including a safety data update, a new package insert and packaging configurations for Trokendi XR and was informed that should the FDA approve such amendment, it will most likely be in the form of a tentative approval because the review period of such amendment would be expected to conclude in the second quarter prior to the June 22, 2013 expiration of the pediatric exclusivity. The Company continues to expect getting the final approval and commercially launching Trokendi XR in the third quarter of 2013. Topiramate is marketed by Johnson & Johnson under the brand name Topamax and is also available in a generic form. Topiramate is currently available only in immediate release form and is indicated for monotherapy and adjunctive therapy of epilepsy and for the treatment of migraine. Topamax reached peak worldwide sales of \$2.7 billion in 2008, before generic products entered the U.S. market in March 2009.⁽¹⁶⁾ With approximately 10 million total topiramate prescriptions in the U.S. in 2011 and 10.6 million prescriptions in 2012, topiramate continues to represent a significant portion of prescriptions with approximately 8.4% of total prescriptions, according to data from IMS Health. Topiramate is believed to work in epilepsy through various mechanisms. It enhances the inhibitory effect of the GABA (gamma-aminobutyric acid) neurotransmitter that regulates neuronal excitability throughout the nervous system, blocks the excitatory effect of the glutamate neurotransmitter, blocks the sodium channel and inhibits the carbonic anhydrase enzyme. The side effects associated with taking topiramate, which have tended to limit its use, include, among others, dizziness, fatigue, somnolence and slowing of certain cognitive functions. We believe that this creates an opportunity for us to offer patients Trokendi XR as an alternative therapy to immediate release topiramate with an improved once-per-day profile.

Trokendi XR is designed to improve patient compliance and to have a better tolerability profile compared to the current immediate release products that are taken multiple times per day. Trokendi XR's pharmacokinetic profile delivers lower peak plasma concentrations and lower input rate over an extended time period resulting in smoother and more consistent blood levels of topiramate during the day compared to immediate release Topamax. We believe such a profile mitigates blood level fluctuations that are typically associated with many of the side effects or breakthrough seizures that patients can suffer when taking immediate release products. These side effects can lead patients to skipping doses, and such non-compliance could place them at higher risk for breakthrough seizures.

Trokendi XR was studied in a U.S. Phase II, multicenter, open-label, sequentially-designed conversion clinical trial among patients between the ages of 18 and 65 having partial-onset or primary generalized seizures. Prior to enrolling in the study, patients were taking topiramate twice-a-day immediate release

(16) Based on sales data as reported in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 3, 2010.

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products with total daily regimen that ranged from 200 mg-400 mg. Patients were first converted to equivalent Topamax twice-a-day immediate release doses for two weeks and then converted to an equivalent once daily dose of Trokendi XR for two more weeks. The study successfully met its primary objective of showing that Trokendi XR is bioequivalent to Topamax immediate release in epilepsy patients. For example, the ratio of dose-normalized (200 mg) geometric least-square means Trokendi XR versus Topamax and the 90% intervals (CIs) were within the bioequivalence criteria of 80-125% for Area under the Curve (AUC) (101.69, 90% CI; 87.10, 118.72), maximum concentration C_{max} (97.30, 90% CI; 84.50, 112.04), and minimum concentration C_{min} (100.59, 90% CI; 83.24, 121.56). Trokendi XR was also well tolerated and the majority of the patients (85.5%) converted from Topamax immediate release to Trokendi XR with no treatment related AEs. There were no serious AEs or deaths and all reported AEs were mild to moderate. There were no notable differences in seizure frequency between the treatments.

When asked two questions at the end of the study about their preference, the sixty-one (61) subjects who completed the study responded as follows:

Which treatment do you prefer? The once-a-day treatment or twice-a-day treatment?

Does the once-a-day treatment (Trokendi XR) help you to be more compliant in taking your medication?

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Trokendi XR Development Program

The FDA issued tentative approval of Trokendi XR in June 2012. We pursued a Section 505(b)(2) regulatory strategy, which allowed us to rely in our NDA filing on the FDA's findings of safety and effectiveness of Topamax. The various clinical trials conducted on Trokendi XR were designed to select the best extended release once-per-day formulation that delivers equivalent levels of topiramate compared to the immediate release twice-per-day Topamax product, as well as to test the robustness and consistency of our technology in delivering the once-per-day formulation across a full range of product strengths. We believe that the data generated by our studies support our Section 505(b)(2) regulatory strategy of establishing Trokendi XR as bioequivalent to Topamax. We also have scaled up production of the product candidate at our commercial contract manufacturing facility and have conducted studies that confirm that the commercial scale product is bio-equivalent to the clinical product that was initially developed at our research laboratories.

Commercialization Strategy

If we are successful in obtaining final regulatory approval, we believe that Trokendi XR will be the first once-daily topiramate product approved in the U.S., as initial monotherapy in patients 10 years of age and older with partial onset or primary generalized tonic-clonic seizures, and as adjunctive therapy in patients 6 years of age and older with partial onset or primary generalized tonic-clonic seizures or with seizures associated with Lennox-Gastaut syndrome. We believe that Trokendi XR could, over time, capture a significant share of the topiramate prescriptions, consistent with the performance of similar extended release products that have been introduced in the U.S. epilepsy market over the past 15 years. As discussed above, we have built our sales and marketing capabilities in the United States to complete the launch of Oxtellar XR. Upon the commercial launch of Trokendi XR, assuming receipt of final approval from the FDA, we expect to further expand our sales and marketing capabilities later this year. We expanded our agreement with the CMO to provide for the production of commercial quantities of Trokendi XR to prepare for the commercial launch of Trokendi XR assuming receipt of final approval by the FDA. In 2012, two U.S patents were issued covering the product.

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.⁽¹⁷⁾ An estimated 50% of children with ADHD continue to meet criteria for ADHD into adolescence.⁽¹⁸⁾ In 2011, the U.S. market for ADHD prescription drugs was more than \$4.4 billion, according to data from Datamonitor.⁽¹⁹⁾

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

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

(19) R & D Trends: *Attention Deficit Hyperactivity Disorder*, published June 2011, at www.datamonitor.com.

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Diagnosis of ADHD requires a comprehensive clinical evaluation based on identifying patients who exhibit the core symptoms of inattention, hyperactivity, and impulsivity. Generally, behavior is sufficiently severe and persistent to cause functional impairment. 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 are treated for ADHD. It is estimated that the annual societal cost of illness for ADHD is more than \$36 billion.(20)

Current Treatment Options

Since Ritalin was introduced, stimulant therapies have grown to become the most common form of treatment for ADHD. Studies indicate that approximately 80% of ADHD patients respond to stimulants.(21) A key difference between older and newer oral stimulants is the duration of action. Most of the older stimulants, representing approximately 35% of total oral stimulant prescriptions based on IMS Health data, are immediate release products that last approximately four hours, requiring multiple administrations throughout the day. In contrast, most of the recently launched products, representing approximately 65% of total oral stimulant prescriptions based on IMS Health data, are extended release formulations that last up to twelve hours or more.

While stimulant treatments calm and improve the concentration of ADHD patients, these drugs have been shown to have various side effects including loss of appetite, insomnia and, to a lesser degree, cardiovascular effects. Stimulant treatments are controlled substances and can be associated with social stigma and the potential for abuse. Approximately 30% of patients with ADHD are non-responsive to or non-tolerant of treatment with stimulants.(22) Non-stimulants offer physicians an alternative ADHD therapy, including for patients who have coexisting conditions, such as conduct disorder, major depressive disorder, or bipolar disorder, that are contraindicated for stimulant use based on the risk for stimulant abuse.

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- (20) Pelham, W.E., *The Economic Impact of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents*, published July 2007 in *Journal of Pediatric Psychology*.
- (21) Swanson, J.M., *Attention-deficit hyperactivity disorder and hyperkinetic disorder*, published February 1998 in *The Lancet* and Budur, K., *Non-Stimulant Treatment for Attention Deficit Hyperactivity Disorder*, published July 2005 in *Psychiatry*.
- (22) Wigal, S.B., *Efficacy and Safety Limitations of Attention-Deficit Hyperactivity Disorder Pharmacotherapy in Children and Adults*, published August 2009 in *CNS Drugs* and Budur, K., *Non-Stimulant Treatment for Attention Deficit Hyperactivity Disorder*, published July 2005 in *Psychiatry*.

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Coexisting Conditions

Studies show that as many as 67% of children who have ADHD may have coexisting conditions such as oppositional defiant disorder, conduct disorder, anxiety disorder and depression.(23) In addition, it has been estimated that approximately 25% of children with ADHD also exhibit persistent conduct problems, such as impulsive aggression.(24) Untreated, these serious conduct problems can place patients at risk of persistent aggressive and anti-social behavior, such as knowingly destroying property, physically attacking people and bullying. These patients also face an increased risk of suicidal behavior, and are at high risk of entering the juvenile justice system and developing substance abuse problems later in adulthood.

Aggression is usually divided into two subtypes: predatory (i.e., "cold") aggression, which can be described as goal-oriented, controlled and/or planned, and impulsive or affective (i.e., "hot") aggression, which can be described as reactive, unplanned and/or uncontrolled. Patients with ADHD who exhibit aggression commonly demonstrate the "hot," or impulsive, type of aggression. For these patients, this "hot" aggression is generally recurrent, occurs outside of a justifiable social context, has intensity, frequency, duration or severity that is disproportionate to its triggers and causes distress and impairment to the patient. Impulsive aggression represents a broad category of maladaptive, aggressive behaviors that can complicate the management of ADHD, autism, bipolar disorder, post-traumatic stress disorder and other psychiatric disorders.

Current Treatments for Impulsive Aggression in Patients with ADHD

Currently, there are no approved medications for treating impulsive aggression in patients with ADHD. The current treatment options for impulsive aggression in patients with ADHD include psychosocial interventions, such as school- or family-based behavioral therapies, which are usually not wholly effective. In the large, multisite Multimodal Treatment Study of Children with ADHD,(25) 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 exhibited initial aggression still had what can be described as impulsive aggression at the end of the trial, demonstrating 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 address this group with 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, lipid abnormalities, and diabetes, which is of particular concern when treating pediatric populations.

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

(24) Jensen, P.S., *Consensus Report on Impulsive Aggression as a Symptom Across Diagnostic Categories in Child Psychiatry: Implications for Medication Studies*, published March 2007 in *Journal of the American Academy of Child and Adolescent Psychiatry*.

(25) 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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Our Psychiatry Portfolio

Our psychiatry portfolio includes three product candidates for the treatment of impulsive aggression in patients with ADHD, ADHD or its coexisting conditions and one product candidate for depression, each of which is designed to bring important advancements in therapy.

SPN-810 (molindone hydrochloride)

We are developing SPN-810 (molindone hydrochloride extended release formulation) as a novel treatment for impulsive aggression in patients with ADHD. We initiated a Phase IIb trial of SPN-810 in the United States in June 2011, for which we received preliminary results in November 2012. The trial's primary objective was to study three different doses of SPN-810 ranging from 12 mg per day to 54 mg per day depending on patients' weight. The study accomplished its objectives of establishing a dose range at which the drug is effective and confirmed the efficacy of SPN-810 in the treatment of impulsive aggression in ADHD patients weighing 30 kg or more. Based on the efficacy demonstrated by the low and medium doses in this study across several measures in these patients, we have decided to advance the program into later stage development. We are continuing to analyze the full dataset in depth and plan to subsequently meet with the FDA to discuss next steps in the development program and the design and protocol for Phase III clinical trials of SPN-810. If approved by the FDA, SPN-810 could be the first product available to address this serious, unmet medical need. We submitted INDs for SPN-810 in 2008 and 2009.

We are studying SPN-810, which contains molindone hydrochloride, as a treatment of impulsive aggression in patients with ADHD. Molindone hydrochloride was previously marketed in the United States as an anti-psychotic to treat schizophrenia under the trade name Moban. Molindone hydrochloride is unusual among anti-psychotics in that it is less likely to be associated with weight gain. In addition, we believe the lower doses tested for the proposed indication of impulsive aggression should be more easily tolerated than the higher doses approved to treat schizophrenia. SPN-810's low potential to cause weight gain leads us to believe that SPN-810 could be an attractive candidate among the anti-psychotic drugs for the effective treatment of impulsive aggression in patients with ADHD. Although initially we are developing SPN-810 as a treatment of impulsive aggression, if we are successful in demonstrating the effectiveness of SPN-810 for the treatment of impulsive aggression in patients with ADHD, we may then look to develop the product candidate for the treatment of other patient populations that have impulsive aggression, such as autism and bipolar disorder.

SPN-810 Development Program

We have completed five clinical trials for SPN-810, including a Phase IIa U.S. trial in which we tested the safety and tolerability of SPN-810, immediate release molindone hydrochloride, in patients with ADHD who suffer from serious persistent conduct problems. This open-label, dose-ranging trial randomized 78 children, 6 to 12 years of age, into one of four treatment groups, which were given four different doses of immediate release molindone hydrochloride, between 10 mg and 40 mg per day, depending on weight, three times a day over a six-week treatment period, after 2-5 weeks of titration. SPN-810 was well tolerated in the trial, with no clinically meaningful changes in standard hematology, clinical chemistry values, vital signs or electrocardiogram, or ECG, results. Besides safety and tolerability assessments, the primary outcome measure was the change in the Nisonger Child Behavior Rating Form-Typical Intelligence Quotient, or NCBRF-TIQ, conduct problem subscale scores from baseline to endpoint in the ITT population. NCBRF-TIQ is a well established instrument that has been used for assessing child and adolescent behavior. Scores improved after baseline in all treatment groups. By visit 12, after 6 weeks of treatment, the mean reduction from baseline values for each treatment group was 7.0, 8.7, 8.2 and 14.3, in groups 1, 2, 3 and 4, respectively, representing decreases of 34%, 34%, 32% and 55%, respectively. In addition, the difference between group 1 and group 4 was statistically significant ($p \leq 0.041$) at all time points except visit 2 and the greatest improvement in scores

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on the NCBRF-TIQ conduct problem subscale was seen in group 4, which was the highest-dose group (14.8 mean reduction). The below chart summarizes the mean change in NCBRF-TIQ conduct problem subscale observed in our Phase IIa trial.

**NCBRF-TIQ Conduct Problem Subscale:
Mean Change From Baseline (ITT Population)**

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**NCBRF-TIQ Conduct Problem Subscale:
Mean Change from Baseline in ITT Population**

Secondary outcomes included changes in other ADHD and conduct problem scales, as described in the table below. SPN-810 demonstrated improved scores over time in all treatment groups, with more marked improvements in higher-dose groups than in lower-dose groups as set out in greater detail in the table below.

**% Improvement from Baseline to Last Visit,
Secondary Outcome Measures (ITT Population)**

Outcome Measure	Treatment Groups			
	Group 1 n=20	Group 2 n=19	Group 3 n=19	Group 4 n=20
CGI-S				
% Improvement	23%	21%	27%	36%
SNAP-IV Subscales				
ADHD Inattention				
% Improvement	24%	31%	34%	39%
ADHD Hyperactivity/Impulsivity				
% Improvement	28%	27%	28%	41%
ADHD-Combined				
% Improvement	26%	29%	31%	40%
ODD				
% Improvement	34%	33%	28%	51%

CGI-S=Clinical Global Impression-Severity Scale, an assessment tool to rate the severity of the condition; ODD=Oppositional Defiant Disorder, a coexisting condition of ADHD; SNAP-IV=Swanson, Nolan and Pelham Questionnaire, a commonly used scale to measure ADHD.

In June 2011, we initiated 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 impulsive aggression that is not controlled by optimal stimulant and behavioral therapy. The primary objective of the study was to assess the effectiveness of SPN-810, extended release, at three different doses in reducing impulsive aggression after at least three weeks of treatment. The primary endpoints were the effect in reducing impulsive aggression as measured by change in the score of the Retrospective Modified Overt Aggression Scale, or R-MOAS, and the rate of remission. Secondary endpoints include measurement of the effectiveness of SPN-810 on Clinical Global Impression and ADHD scales as well as evaluation of the safety and tolerability of the drug. In addition, we are exploring the potential added advantages of an extended-release formulation, such as greater compliance and, therefore, effectiveness in school-age children and lower unwanted side effects or interpatient variability. Patients who completed the study were offered the opportunity to continue into an open-label phase of six months duration. We received preliminary results in November 2012.

For all patients, low and medium doses of SPN-810 met the efficacy endpoint of rate of remission of aggression and showed statistical significance versus placebo with p-values of 0.009 and 0.043 and percent of patients with R-MOAS remission of 51.9% and 40.0%, respectively. The low and medium doses showed a reduction in score for the R-MOAS of 62.6% and 57.9%, respectively, with p-values of 0.071 and 0.115.

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For patients of 30 kg or more in weight, the low and medium doses of SPN-810 showed statistical significance versus placebo on the change in R-MOAS primary endpoint with p-values of 0.024 and 0.049, and high percent reduction in the R-MOAS scores of 80.9% and 75.2%, respectively. In addition, both doses resulted in remission of aggression with statistical significance versus placebo with p-values of 0.004 and 0.021 with percent of patients with R-MOAS remission of 66.7% and 53.3%, respectively. The low dose also met the secondary endpoints of Clinical Global Impression, or CGI, for Severity and Improvement, and of the Swanson, Nolan and Pelham Rating Scale, or SNAP-IV, rating for Oppositional Defiant Disorder with statistical significance versus placebo with p-values of 0.007, 0.017 and 0.039, respectively, and improvements of 41.3%, 34.5% and 49.3%. The high dose did not show statistically significant efficacy across any of these measures.

For patients under 30 kg in weight, while the low and medium doses showed improvements over placebo in the primary endpoints and the SNAP-IV rating for Oppositional Defiant Disorder, the studied doses did not show statistical significance versus placebo on efficacy measures. Coupled with the fact that the high dose did not show efficacy with statistical significance, this unexpected result leads us to believe that the most effective doses are those that achieve certain plasma concentrations (related to body weight) that do not exceed a level beyond which some sort of saturation threshold is reached.

Efficacy in Patients \geq 30 kg on Low to Medium Doses**Primary Efficacy Endpoints**

(Treatment vs. placebo in ITT population)	Placebo	Low Dose	Medium Dose	High Dose
R-MOAS Change Overall (% improvement)	(38.5)	(62.6)	(57.9)	(39.7)
Patients (<30kg)	(35.3)	(42.3)	(44.4)	(33.7)
Patients (\geq 30kg)	(41.5)	(80.9)	(75.2)	(44.4)
R-MOAS Remission Overall (% of patients)	(20.0)	(51.9)	(40.0)	(32.3)
Patients (<30kg)	(25.0)	(33.3)	(26.7)	(21.4)
Patients (\geq 30kg)	(16.7)	(66.7)	(53.3)	(41.2)

R-MOAS=Retrospective-Modified Overt Aggression Scale; R-MOAS Change=from Baseline (Visit 5) to Endpoint (Visit 10); R-MOAS Remission=Score of \leq 10 (LOCF=Last Observation Carried Forward) at Endpoint (Visit 10)

Efficacy in Patients \geq 30 kg on Low to Medium Doses**Primary Efficacy Endpoints**

(Treatment vs. placebo in ITT population)	Placebo	Low Dose	Medium Dose	High Dose
R-MOAS Change Overall (% improvement)	(38.5)	(62.6)	(57.9)	(39.7)
Patients (<30kg)	(35.3)	(42.3)	(44.4)	(33.7)
Patients (\geq 30kg)	(41.5)	(80.9)	(75.2)	(44.4)
R-MOAS Remission Overall (% of patients)	(20.0)	(51.9)	(40.0)	(32.3)
Patients (<30kg)	(25.0)	(33.3)	(26.7)	(21.4)
Patients (\geq 30kg)	(16.7)	(66.7)	(53.3)	(41.2)

R-MOAS=Retrospective-Modified Overt Aggression Scale; R-MOAS Change=from Baseline (Visit 5) to Endpoint (Visit 10); R-MOAS Remission=Score of \leq 10 (LOCF=Last Observation Carried Forward) at Endpoint (Visit 10)

Table of Contents**Statistical Significance in Patients \geq 30 kg on Low Dose**

Secondary Efficacy Endpoints (Treatment vs. placebo in ITT population)	Low Dose P-value	Medium Dose P-value	High Dose P-value
CGI-Severity Overall	0.133	0.308	0.245
Patients (<30kg)	0.42	0.839	0.946
Patients (\geq 30kg)	0.007	0.117	0.125
CGI-Improvement Overall	0.175	0.061	0.888
Patients (<30kg)	0.494	0.664	0.756
Patients (\geq 30kg)	0.017	0.028	0.654
SNAP-IV ODD Subscale Overall	0.061	0.122	0.661
Patients (<30kg)	0.639	0.173	0.607
Patients (\geq 30kg)	0.039	0.179	0.861

CGI=Clinical Global Impression; SNAP-IV=Swanson, Nolan and Pelham, ADHD Rating Scale; ODD=Oppositional Defiant Disorder

Efficacy in Patients \geq 30 kg on Low Doses

Secondary Efficacy Endpoints (Treatment vs. placebo in ITT population)	Placebo	Low Dose	Medium Dose	High Dose
CGI-Severity Overall (% improvement)	19.6	28.2	25.5	26.7
Patients (<30kg)	22.9	17.0	22.4	23.9
Patients (\geq 30kg)	15.9	41.3	31.1	29.5
CGI-Improvement Overall (% improvement)	15.1	20.0	28.1	18.2
Patients (<30kg)	15.1	6.2	23.5	12.5
Patients (\geq 30kg)	15.1	34.5	35.5	21.2
SNAP-IV ODD Subscale Overall (% improvement)	18.0	34.4	30.3	21.4
Patients (<30kg)	12.8	17.4	23.2	17.9
Patients (\geq 30kg)	21.5	49.3	39.3	24.2

CGI=Clinical Global Impression; SNAP-IV=Swanson, Nolan and Pelham, ADHD Rating Scale; ODD=Oppositional Defiant Disorder

We will be conducting further analyses of the full dataset including analyzing the pharmacokinetic and pharmacodynamic relationship from the pharmacokinetic data generated from the study at various doses for patients in different weight groups.

SPN-810 was well tolerated throughout the study across all doses. 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 high dose. Analysis of all safety and clinical lab data has not yet been completed, though SPN-810 seemed to have a good safety and tolerability profile.

Table of Contents**Safe and Well Tolerated**

Number (%) of Patients with:	Placebo	Low Dose	Medium Dose	High Dose
Any adverse event (AE)	18 (58.1)	11 (37.9)	18 (60.0)	21 (67.7)
Adverse reaction	7 (22.6)	6 (20.7)	11 (36.7)	13 (41.9)
Severe AEs	0 (0.0)	1 (3.4)	4 (13.3)	1 (3.2)
Severe Adverse Reaction	0 (0.0)	1 (3.4)	2 (6.7)	0 (0.0)
Any serious AE (SAE)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.2)
Serious Adverse Reaction	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
AEs leading to discontinuation	1 (3.2)	1 (3.4)	2 (6.7)	3 (9.7)

Adverse Reaction=those AEs considered possibly or definitely study drug related, according to investigator

Safe and Well Tolerated

Adverse Reaction (%) of Patients	Placebo	Low	Medium	High
Decreased appetite	0	0	3.3	6.5
Increased appetite	3.2	6.9	6.7	6.5
Sedation	6.5	6.9	6.7	6.5
Somnolence	3.2	0	0	6.5
Fatigue	0	0	0	9.7
Dystonia	0	0	6.7	0

Adverse Reactions in $\geq 5\%$ of patients across Titration & Maintenance Periods

SPN-812

We are developing SPN-812, which is currently in Phase II development, as a novel non-stimulant treatment for ADHD. SPN-812 is a selective norepinephrine reuptake inhibitor that we believe could be more effective and have a better side effect profile than other non-stimulant treatments for ADHD. The active ingredient in SPN-812 has an extensive safety record in Europe, where it was previously marketed for many years as an anti-depressant. SPN-812 has not been developed and marketed in the United States and, therefore, it would be considered and reviewed by the FDA as an NCE. We submitted one IND for SPN-812 in 2010.

SPN-812 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 different pharmacological profile. Due to its demonstrated efficacy as an anti-depressant, SPN-812, if studied in that specific patient population and shown to be effective, may exhibit increased benefit in up to an estimated 40% of ADHD patients who also suffer from major depression.⁽²⁶⁾ We are developing an intellectual property position around the novel synthesis process for this product candidate, its novel use in ADHD and its novel delivery with extended release.

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Biederman, J., *New Insights Into the Comorbidity Between ADHD and Major Depression in Adolescent and Young Adult Females*, published in April 2008 in *Journal of the American Academy of Child and Adolescent Psychiatry* and Report of CME Institute of Physicians Postgraduate Press, Inc., published in August 2008 in *Journal of Clinical Psychiatry*.

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SPN-812 Development Program

We completed a proof-of-concept Phase IIa U.S. clinical trial of SPN-812 in adults for the treatment of ADHD in 2011, in which SPN-812 was well tolerated and demonstrated a statistically significant improvement over placebo as a treatment for ADHD. The trial met the primary endpoints of safety and tolerability, and showed statistically significant median reduction versus placebo in both investigator-rated and patient-rated ADHD symptom scores. The trial was a randomized, double-blind, placebo-controlled trial in 52 adults with a current diagnosis of ADHD (26 subjects per treatment group).

Patients in the active arm were administered SPN-812 at a single dose level three times a day over five weeks, after a one-week titration phase. The primary endpoint was safety, and SPN-812 was shown to be safe and well tolerated by patients. The secondary endpoints included: the efficacy of SPN-812 as measured by Total ADHD Symptom Score on the Conners' Adult ADHD Rating Scale, or CAARS, a commonly-used measurement for ADHD in adults, as rated by each of the investigators and the patients, and the effectiveness of SPN-812 when compared to placebo as determined by changes in the CGI Improvement, or CGI-I, score. Patients in the active group achieved overall significant median reductions from baseline in investigator-rated CAARS total ADHD symptom scores by study end, of 11.5 points versus 6.0 points for placebo ($p=0.0414$) and in self-rated CAARS total symptom scores by study end, of 10.5 points versus 1.0 for placebo ($p=0.0349$). With respect to the other secondary endpoint of CGI-I scores, patients exhibited a trend, although not statistically significant, toward larger median reductions in scores from baseline versus placebo.

Given the positive results of this Phase IIa trial, we are focused on developing an extended release formulation that will be the subject of a future Phase IIb trial.

SPN-809

We are developing SPN-809 as a novel once-daily product candidate for the treatment of depression. SPN-809 is based on the same active ingredient as SPN-812. We currently have an open IND for SPN-809 as a treatment of depression, the indication for which the active ingredient in SPN-809 was approved and marketed in Europe for many years. Depression is a serious and common disease affecting approximately 121 million people worldwide.⁽²⁷⁾ Based on IMS Health data, the worldwide market for anti-depressants is approximately \$12 billion.

SPN-809 is a norepinephrine reuptake inhibitor that represents an opportunity to offer a differentiated treatment option for patients suffering from depression in the United States. Initial market research suggests that psychiatrists would like to have such a once-daily option at their disposal to treat various patients. 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.

Other Product Candidates

We have additional product candidates in various stages of early development that cover a range of CNS disorders.

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 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 meet efficacy needs, more convenient and less frequent

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World Health Organization, *Epilepsy: aetiology, epidemiology and prognosis*, Fact Sheet No. 165, revised February 2001.

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dosing, enhanced patient compliance, and improved tolerability in certain specific applications. Our broad portfolio of technologies and extensive expertise in this area, built over the past 20 years, enable us to develop products that are technically difficult to formulate and by design are harder for others to copy. We have employed our technologies in the development of our legacy products, as well as in our current product portfolio.

Microtrol (multiparticulate delivery platform)

Microtrol is based on the use of coated and uncoated multi-particulates that can be filled into capsules, administered as a sprinkle, or compressed into tablets as varying ratios to achieve novel customized release profiles. The following approved and marketed products incorporate our Microtrol technology:

Sanctura XR (trospium chloride), a treatment for overactive bladder;

Oracea (doxycycline), a treatment for inflammatory lesions of rosacea;

Carbatrol (carbamazepine), an anti-epilepsy treatment;

Equetro (carbamazepine), a treatment for bipolar disorder; and

Adderall XR (mixed amphetamine salts), a stimulant ADHD treatment.

We do not expect the above products to contribute to our future financial position. Carbatrol, Equetro and Adderall XR are legacy products that were developed by us when we were formerly Shire Laboratories. In addition, in April 2008, we monetized the revenues underlying the future royalty streams relating to Sanctura XR and Oracea by transferring certain of our royalty payment rights and other license rights for such products to TCD Royalty Sub LLC, or Royalty Sub, in exchange for \$63 million. We primarily reinvested the proceeds from this transaction into our research and development activities. In December 2011, we sold 100% of our equity ownership interests in Royalty Sub. See "Management's Discussion and Analysis of Financial Condition and Results of Operations History of our Company" and Note 10 of the audited financial statements for additional details regarding the sale of Royalty Sub.

Solutrol (matrix delivery platform)

Solutrol is a matrix delivery system that can deliver poorly soluble, highly soluble, and pH dependent compounds in a reproducible and complete manner. Solutrol has been incorporated into Intuniv (guanfacine), a nonstimulant ADHD treatment, which is currently licensed to and marketed by Shire plc. In April 2009, this license became fully paid up when we sold to Shire the right to receive royalties and milestone payments owed to us for \$36.9 million, which we primarily reinvested into our research and development activities.

EnSoTrol (osmotic delivery system)

EnSoTrol is comprised of a solubility enabled core and other agents surrounded by a semi-permeable membrane with a laser-drilled hole. When EnSoTrol is introduced to the contents of the gastrointestinal tract, it will induce solubilization of the core contents via fluid intake across the membrane coating. The solubilized core contents are then released through the laser-drilled hole along the osmotic gradient, thus yielding a surface-area controlled constant release profile. EnSoTrol has been tested in several clinical trials, including Phase III trials conducted by United Therapeutics for an oral formulation of tadalafil, or tadalafil that is the subject of an NDA.

In June 2006, we entered into a license agreement with United Therapeutics Corporation, or United Therapeutics, for the worldwide development and commercialization of an oral formulation of tadalafil, which utilizes EnSoTrol for the treatment of pulmonary arterial hypertension, or PAH, as well as for other indications. Under the terms of the license agreement, we have received

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pre-commercial milestone payments of \$1.5 million. Remaining milestone payments to us could total up to approximately \$6.0 million, which includes milestone payments that could total \$2.0 million based on the satisfaction of development milestones of oral treprostinil in PAH and up to approximately \$4.0 million for the development of additional treprostinil products for a second indication. If United Therapeutics receives approval to market and sell an oral formulation of treprostinil, we will be entitled to receive royalties in the single digits based on net sales worldwide. On October 23, 2012, the FDA issued a complete response letter declining approval of the product. We do not expect to receive any royalties for this oral formulation unless and until final marketing approval from the FDA is received and United Therapeutics launches this product. Our license agreement with United Therapeutics will expire, on a country-by-country and product-by-product basis, 12.5 years from the first commercial sale of each product in such country. United Therapeutics may terminate, at its option, the agreement for a technical, strategic or market-related cause after giving us a reasonable opportunity to cure. We may terminate the agreement if, after having launched a product in a country, United Therapeutics or its sublicensee discontinues the sale of such product for a prolonged period of time for reasons unrelated to force majeure, regulatory or safety issues. In addition, either party may terminate the agreement for the material, uncured breach by the other party and in certain events of bankruptcy or insolvency of the other party.

Other Technologies

We also have proprietary techniques for identifying lead molecules and optimizing their oral delivery consisting of ProScreen, ProPhile and OptiScreen technologies. ProScreen is a predictive screen for lead candidates that warrant oral delivery. ProPhile is a suite of in silico modeling tools that enables multivariate analysis and pharmacokinetic prediction. OptiScreen is a technology for formulation optimization including solubility or permeability enhancement leading to oral bioavailability improvement. We believe that this suite of technologies enables us to optimize the delivery and the development of existing chemical entities and marketed products.

Sales and Marketing

We have built our sales and marketing capabilities in the United States to launch Oxtellar XR and, assuming receipt of final approval from the FDA, Trokendi XR. Additionally, there are plans to further expand our sales and marketing capabilities later this year. Having two epilepsy products that can be promoted to the same physician audience would allow us to leverage our commercial infrastructure with these prescribers. Once we have obtained approval for any of our product candidates in our psychiatry portfolio, we anticipate adding additional sales force members who will be dedicated to marketing our psychiatry products.

Manufacturing

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 depend on third-party CMOs for all of our required raw materials and drug substance for our preclinical research and clinical trials. We do not have contractual relationships for the commercial manufacture of all our product candidates. For Trokendi XR, Oxtellar XR and our product candidates, we currently rely on single third-party suppliers for raw materials including drug substance and single manufacturers for the final commercial products. We currently employ internal resources and as needed third-party consultants to manage our manufacturing contractors.

For both Oxtellar XR and Trokendi XR, we have entered into agreements with leading CMOs headquartered in North America for the manufacture of the final commercial products. They offer a comprehensive range of contract manufacturing and packaging services and have successfully handled

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the scale up of Oxtellar XR to a commercial production scale and will scale up commercial production of Trokendi XR in preparation for commercialization of this product, assuming final FDA approval.

Competition

The biotechnology and pharmaceutical industries are highly competitive. A number of multinational pharmaceutical companies as well as large biotechnology companies are pursuing the development of or are currently marketing pharmaceutical products in the anti-epilepsy and ADHD markets on which we are focusing.

Epilepsy

There are currently over 15 branded products, as well as their generic counterparts, on the U.S. market indicated to treat some form of epilepsy. Several NCEs have entered the epilepsy market including Potiga, Vimpat and Banzel. Another NCE, Stedesa, could be approved later in 2013 and enter the market thereafter. Based on IMS Health prescription data from 1994 to 2005 for NCE launches for seizure disorders, such NCEs, on average, experienced slow market penetration characterized by a 0.58% to 1.1% market share point gain on an annual basis. We believe this is because physicians are often reluctant to change a stable patient's existing therapy and risk a breakthrough seizure in their patients.

Oxtellar XR competes with all immediate release oxcarbazepine products including Trileptal and related generic products. We are not aware of any other company that is currently developing an extended release oxcarbazepine anti-epileptic product in the United States. In addition, we believe that Oxtellar XR's once-daily formulation solves a drug delivery challenge specific to oxcarbazepine that must be overcome by all potential competitors. We are aware of companies who have modified-release oxcarbazepine products that are marketed outside of the United States but, to our knowledge, such products are not being pursued for the U.S. market. These modified-release oxcarbazepine products include Apydan, which is developed by Desitin Arzneimittel GmbH, and requires twice-daily administration.

If final approval is received, Trokendi XR will compete with all immediate release topiramate products including Topamax and related generic products. We are aware that Upsher-Smith Laboratories, Inc., or Upsher-Smith, conducted a Phase III clinical trial for an extended release topiramate product, which it has described as an internally developed program for the management of epilepsy in adults using its proprietary formulation technology. If this product candidate is approved by the FDA before Trokendi XR, then Upsher-Smith could obtain three years of marketing exclusivity, which would significantly delay our entry into the U.S. market.

ADHD

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. Shire plc is one of the leaders in the U.S. ADHD market with three products: Adderall XR, an extended release stimulant treatment designed to provide once-daily dosing; Vyvanse, a stimulant prodrug product launched in 2007; and Intuniv, a non-stimulant treatment launched in November 2009. Other stimulant products for the treatment of ADHD in the U.S. market include the following once-daily formulations: Concerta; Metadate CD; Ritalin LA; Focalin XR; and Daytrana. Other non-stimulants are Strattera and Kapvay. We are also aware of clinical development efforts by several large pharmaceutical companies including Eli Lilly, Otsuka America, Inc., BMS, AstraZeneca plc and Abbott Laboratories to develop additional treatment options for ADHD.

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Intellectual Property and Exclusivity

Overview

We have been building and continue to build our intellectual property portfolio relating to our products and product candidates, including Oxtellar XR and Trokendi XR. We seek patent protection, where appropriate, in the United States 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 United States and abroad (including Europe, Canada and certain other countries when appropriate) relating to proprietary technologies that are important to the development of our business. 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, defend our patents, 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 technologies in the United States and abroad.

Patent Portfolio

Our extended release oxcarbazepine patent portfolio currently includes four U.S. patents, two of which cover Oxtellar XR. We have also obtained two patents for extended release oxcarbazepine in Europe, one patent in Canada and one patent in Mexico. In addition, we have certain pending U.S. and foreign patent applications that are directed to various extended release formulations containing oxcarbazepine. The issued U.S. patents covering Oxtellar XR will expire in 2027. We own all of the issued patents and the pending applications.

In addition to the patents and patent applications relating to Oxtellar XR, we currently have two U.S. patents that cover Trokendi XR. We have one patent issued in Europe for extended release topiramate and have certain pending U.S. and foreign patent applications in Canada and other countries that relate to the U.S. patents directed to various extended release formulations containing topiramate. The two issued U.S. patents will expire in 2027 and 2029, respectively. We own all of the issued patents and pending applications.

Our patent portfolio also contains patent applications relating to our other pipeline products. We have two families of pending U.S. non-provisional and foreign counterpart patent applications relating to our SPN-810 product candidate. Patents, if issued, from the applications could have terms expiring from 2029 to 2031. 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, from the applications could expire from 2029 to 2033.

The U.S. patent system permits the filing of provisional and non-provisional patent applications. A non-provisional patent application is examined by the U.S. Patent and Trademark Office, or USPTO, and can mature into a patent once the USPTO determines that the claimed invention meets the standards for patentability. A provisional patent application is not examined for patentability, and automatically expires 12 months after its filing date. As a result, a provisional patent application cannot mature into a patent. The requirements for filing a provisional patent application are not as strict as those for filing a non-provisional patent application. Provisional applications are often used, among other things, to establish an early filing date for a subsequent non-provisional patent application. The term of individual

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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 United States, a patent's term may be lengthened by patent term adjustment, or 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 where the USPTO erred in calculating the PTA for the patents in question 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.

The filing date of a non-provisional patent application is used by the USPTO to determine what information is prior art when it considers the patentability of a claimed invention. 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, or 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 and 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-812 product candidate and issuance of a U.S. patent covering SPN-812 based on a U.S. patent application in our portfolio, we may obtain a U.S. patent that is eligible for limited patent term restoration.

Other Intellectual Property Rights

We seek trademark protection in the United States 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 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®," "ProScreen®," "OptiScreen®," "ProPhile®," "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 intellectual property 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 intellectual property. For example, where a third party holds relevant intellectual property and is a direct competitor, a license might not be available on commercially reasonable terms or available at all. We strive to identify potential third party intellectual property 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. Litigation to enforce our own patent rights is subject to uncertainties that cannot be quantified in advance. In the case of an adverse outcome in litigation, we could be

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prevented from commercializing a product or using certain aspects of our technology platforms as a result of patent infringement claims 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 "Risk Factors" If we are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in that litigation would have a material adverse effect on our business."

In-Licensing Arrangements

Afecta Pharmaceuticals, Inc.

We have entered into two license agreements with Afecta Pharmaceuticals, Inc., or Afecta, pursuant to which we obtained an exclusive option to evaluate Afecta's CNS pipeline and to obtain exclusive worldwide rights to selected product candidates, including an exclusive license to SPN-810. Under the terms of the license agreements, we have paid Afecta \$550,000 in license fees and milestone payments and may pay up to an additional \$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 based on net sales worldwide in the low-single digits. Unless terminated by us or Afecta for material breach or bankruptcy, by Afecta for our discontinuation of development and commercialization activities, or by us for convenience, the license agreements will continue in full force and effect on a country-by-country basis until six months from the discontinuation of the commercial sale and collection of revenues for the Afecta product.

Rune Healthcare Limited

In June 2006, we entered into a purchase and sale agreement with Rune Healthcare Limited, or Rune, where we obtained the exclusive worldwide rights to a product concept from Rune for SPN-809. Under the terms of the agreement, we have paid Rune a £25,000 up-front fee. If we receive approval to market and sell any products based on the Rune product concept, we will be obligated to pay royalties to Rune based on net sales worldwide in the low-single digits. Unless terminated by us or Rune for material breach, by Rune for our discontinuation of development or commercialization activities relating to a product based on the Rune product concept, we will be obligated to pay royalties to Rune on a country-by-country basis until the earlier of (a) ten years from the date of first commercial sale of a product based on the Rune product concept, or (b) the market entry in such country of any product utilizing the Rune product by any entity other than us, our affiliates or our licensees.

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.

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Government Regulation

Product Approval

Government authorities in the United States at the federal, state and local level, and other countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, recordkeeping, promotion, advertising, distribution, marketing, export and import of products such as those we are developing. Our tentatively approved products and product candidates, including Trokendi XR, must receive final approval from the FDA before they may be marketed legally in the United States.

U.S. Drug Development Process

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and through implementation of regulations. The process of obtaining regulatory approvals and ensuring compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process, or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls, product seizures, product detention, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

completion of preclinical laboratory tests, animal studies and formulation studies according to Good Laboratory Practices regulations;

submission to the FDA of an IND, which must become effective before human clinical trials may begin;

performance of adequate and well-controlled human clinical trials according to Good Clinical Practices, or GCP, to establish the safety and efficacy of the proposed drug for its intended use;

submission to the FDA of an NDA for a new drug;

satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current Good Manufacturing Practices, or cGMP; and

FDA review and approval of the NDA.

The testing and approval process require substantial time, effort and financial resources and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all.

Once a pharmaceutical product candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity, formulation and stability, as well as animal studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, to the FDA as part of the IND. The sponsor must also include a protocol detailing, among other things, the objectives of the initial clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the initial clinical trial lends itself to an efficacy evaluation. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA places the clinical trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve

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any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during trials due to safety concerns or non-compliance.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCP regulations. These regulations include the requirement that all research subjects provide informed consent. Further, an institutional review board, or IRB, must review and approve the plan for any clinical trial before it commences at any institution. An IRB considers, among other things, whether the risks to individuals participating in the trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the information regarding the clinical trial and the consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed.

Once an IND is in effect, each new clinical protocol and any amendments to the protocol must be submitted to the IND for FDA review, and to the IRBs for approval. Protocols detail, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety.

Human clinical trials for product candidates are typically conducted in three sequential phases that may overlap or be combined:

Phase I. The product is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing may be conducted in patients.

Phase II. Phase II trials involve investigations in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage and schedule.

Phase III. In Phase III, clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical trial sites. These trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for regulatory approval and product labeling.

Phase I, Phase II and Phase III testing may not be completed successfully within any specified period, if at all. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and safety reports must be submitted to the FDA and the investigators for serious and unexpected side effects. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product candidate and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

During the development of a new drug, a sponsor may be able to request a Special Protocol Assessment, or SPA, the purpose of which is to reach agreement with the FDA on the Phase III clinical

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trial protocol design and analysis that will form the primary basis of an efficacy claim. An SPA is intended to provide assurance that if the agreed upon clinical trial protocol is followed, the clinical trial endpoints are achieved, and there is a favorable risk-benefit profile, the data may serve as the primary basis for an efficacy claim in support of an NDA. However, SPA agreements are not a guarantee of an approval of a product candidate or any permissible claims about the product candidate. In particular, SPAs are not binding on the FDA if previously unrecognized public health concerns arise during the performance of the clinical trial, other new scientific concerns regarding the product candidate's safety or efficacy arise, or if the sponsoring company fails to comply with the agreed upon clinical trial protocol.

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 an NDA for a new drug, requesting approval to market the product.

As an alternate path to FDA approval, particularly for modifications to drug products previously approved by the FDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments, and 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 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.

The submission of an NDA is subject to the payment of a substantial user fee; a waiver of such fee may be obtained under certain limited circumstances. For example, the agency will waive the application fee for the first human drug application that a small business or its affiliate submits for review.

In addition, under the Pediatric Research Equity Act of 2003, or PREA, which was reauthorized under the Food and Drug Administration Safety and Innovation Act of 2012, an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted. Pursuant to the FDA's approval of Oxtellar XR, we must conduct four pediatric post-marketing studies; however, the FDA granted a waiver for the pediatric study requirements for ages birth to one month and a deferral for submission of post-marketing assessments for children 1 month to 6 years of age.

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,

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commonly referred to as the Orange Book. Specifically, the applicant must certify for each listed patent that (1) the required patent information has not been filed; (2) the listed patent has expired; (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 will also 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, 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.

If the Section 505(b)(2) NDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also 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 after the Section 505(b)(2) NDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement suit against the Section 505(b)(2) applicant. Under the FDCA, the filing of a patent infringement lawsuit within 45 days of receipt of the notification regarding a Paragraph IV certification automatically prevents the FDA from approving the Section 505(b)(2) NDA for 30 months beginning on the date the patent holder receives notice, or until a court deems the patent unenforceable, invalid or not infringed, whichever is earlier. Moreover, in cases where a Section 505(b)(2) application containing a Paragraph IV certification is submitted after the fourth year of a previously approved drug's five year exclusivity period and the patent holder brings suit within 45 days of notice of certification, the 30-month period is automatically extended to prevent approval of the Section 505(b)(2) application until the date that is seven and one-half years after approval of the previously approved reference product. The court also has the ability to shorten or lengthen either the 30 month or the seven and one-half year period if either party is found not to be reasonably cooperating in expediting the litigation. Thus, 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.

We pursued a regulatory strategy pursuant to Section 505(b)(2) in connection with our NDA submissions for Oxtellar XR and Trokendi XR. In the NDA submissions for our other product candidates, we intend to follow the development and approval pathway permitted under the FDCA that we believe will maximize their commercial opportunities.

FDA Review of New Drug Applications

The FDA reviews all NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be re-submitted with the additional information. The re-submitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an

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NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The FDA may refer the NDA to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions. An advisory committee is a panel of independent experts who provide advice and recommendations when requested by the FDA on matters of importance that come before the agency. The FDA is not bound by the recommendation of an advisory committee.

The approval process is lengthy and difficult and the FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical data or other data and information. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. The FDA will issue a complete response letter if the agency decides not to approve the NDA in its present form. The complete response letter usually describes all of the specific deficiencies that the FDA identified in the NDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, withdraw the application, or request an opportunity for a hearing.

If a product receives regulatory approval, the approval may be significantly 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 effectiveness 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 patent term extension under the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term 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. In the future, we intend to apply for restorations of patent term for some of our currently owned or licensed patents to add patent life beyond their current expiration dates, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA.

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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 United States 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, or API, or active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or 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. However, the FDCA will not prevent the submission or approval of another full Section 505(b)(1) NDA, but such an NDA applicant would be required to conduct its own preclinical and adequate, well-controlled clinical trials to demonstrate safety and effectiveness. Further, a Section 505(b)(2) application may be submitted after four years if it contains a Paragraph IV certification. 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 administration or strengths of an existing drug, or for a new use, if 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, which is 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 generic product or 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 in the United States. 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.

Post-Approval Requirements

Any drugs for which we receive FDA approval are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of AEs with the product, providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with FDA promotion and advertising requirements. In September 2007, the Food and Drug Administration Amendments Act of 2007 was enacted, giving the FDA enhanced post-marketing authority, including the authority to require post-marketing studies and clinical trials, labeling changes based on new safety information, and compliance with risk evaluations and mitigation strategies approved by the FDA. The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. Further, manufacturers of drugs must continue to comply with cGMP requirements, which are extensive and require considerable time, resources and ongoing investment to ensure compliance. In addition, changes to the manufacturing process generally require

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prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

Drug manufacturers and other entities involved in the manufacturing and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. The cGMP requirements apply to all stages of the manufacturing process, including the production, processing, sterilization, packaging, labeling, storage and shipment of the drug. Manufacturers must establish validated systems to ensure that products meet specifications and regulatory standards, and test each product batch or lot prior to its release. We rely, and expect to continue to rely, on third parties for the production of clinical quantities of our product candidates. Future FDA and state inspections may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution or may require substantial resources to correct.

The FDA may withdraw a product approval if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. Further, the failure to maintain compliance with regulatory requirements may result in administrative or judicial actions, such as fines, warning letters, holds on clinical trials, product recalls or seizures, product detention or refusal to permit the import or export of products, refusal to approve pending applications or supplements, restrictions on marketing or manufacturing, injunctions or civil or criminal penalties.

From time to time, legislation is drafted, introduced and passed by the United States Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. For example, in July 2012, the Food and Drug Administration Safety and Innovation Act was enacted, expanding drug supply chain requirements and strengthening FDA's response to drug shortages, among other things. In addition to new legislation, the FDA regulations and policies are often revised or reinterpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether further legislative or FDA regulation or policy changes will be enacted or implemented and what the impact of such changes, if any, may be.

Foreign Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our product candidates to the extent we choose to clinically evaluate or sell any products outside of the United States. Whether or not we obtain FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country. As in the United States, post-approval regulatory requirements, such as those regarding product manufacture, marketing, or distribution would apply to any product that is approved outside the United States.

Third-Party Payor Coverage and Reimbursement

In both the United States and foreign markets, our ability to commercialize our product candidates successfully, and to attract commercialization partners for our product candidates, depends in significant part on the availability of adequate financial coverage and reimbursement from third party

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payors, including, in the United States, governmental payors such as the Medicare and Medicaid programs, managed care organizations, and private health insurers. Medicare is a federally funded program managed by the Centers for Medicare and Medicaid Services, or CMS, through local fiscal intermediaries and carriers that administer coverage and reimbursement for certain healthcare items and services furnished to the elderly and disabled. Medicaid is an insurance program for certain categories of patients whose income and assets fall below state defined levels and who are otherwise uninsured that is both federally and state funded and managed by each state. The federal government sets general guidelines for Medicaid and each state creates specific regulations that govern its individual program. Each payor has its own process and standards for determining whether it will cover and reimburse a procedure or particular product. Private payors often rely on the lead of the governmental payors in rendering coverage and reimbursement determinations. Therefore, achieving favorable CMS coverage and reimbursement is usually a significant gating issue for successful introduction of a new product. The competitive position of some of our products will depend, in part, upon the extent of coverage and adequate reimbursement for such products and for the procedures in which such products are used. Prices at which we or our customers seek reimbursement for our product candidates can be subject to challenge, reduction or denial by the government and other payors.

The United States Congress and state legislatures may, from time to time, propose and adopt initiatives aimed at cost containment, which could impact our ability to sell our products profitably. For example, in March 2010, President Obama signed into law the Patient Protection and Affordable Care Act as amended by the Healthcare and Education Affordability Reconciliation Act of 2010, which we refer to collectively as the Health Care Reform Law, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Effective October 1, 2010, the Health Care Reform Law revises the definition of "average manufacturer price" for reporting purposes, which could increase the amount of Medicaid drug rebates to states once the provision is effective. Further, beginning in 2011, the new law imposes a significant annual fee on companies that manufacture or import branded prescription drug products. Substantial new provisions affecting compliance have also been enacted, which may require us to modify our business practices with healthcare practitioners. We will not know the full effects of the Health Care Reform Law until applicable federal and state agencies issue regulations or guidance under the new law. Although it is too early to determine the effect of the Health Care Reform Law, the new law appears likely to continue the pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs. Moreover, in the coming years, additional changes could be made to governmental healthcare programs that could significantly impact the success of our product candidates.

The cost of pharmaceuticals continues to generate substantial governmental and third party payor interest. We expect that the pharmaceutical industry will experience pricing pressures due to the trend toward managed healthcare, the increasing influence of managed care organizations and additional legislative proposals. Our results of operations could be adversely affected by current and future healthcare reforms.

Some third party payors also require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers that use such therapies. While we cannot predict whether any proposed cost-containment measures will be adopted or otherwise implemented in the future, the announcement or adoption of these proposals could have a material adverse effect on our ability to obtain adequate prices for our product candidates and operate profitably.

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Other Healthcare Laws and Compliance Requirements

In the United States, our activities are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including the CMS, other divisions of the U.S. Department of Health and Human Services (e.g., the Office of Inspector General), the U.S. Department of Justice and individual U.S. Attorney offices within the Department of Justice, and state and local governments. These regulations include:

the federal healthcare program anti-kickback law, which prohibits, among other things, persons from soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs;

federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other government reimbursement programs that are false or fraudulent, and which may apply to entities like us which provide coding and billing advice to customers;

the federal Health Insurance Portability and Accountability Act of 1996, which prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters and which also imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information;

the federal transparency requirements under the Health Care Reform Law requires manufacturers of drugs, devices, biologics, and medical supplies to report to the Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests;

the FDCA, which among other things, strictly regulates drug product marketing, prohibits manufacturers from marketing drug products for off-label use and regulates the distribution of drug samples; and

state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by federal laws, thus complicating compliance efforts.

Employees

As of February 28, 2013, we employed 193 full-time employees, up from 110 full-time employees as of December 31, 2012. Approximately 54 employees are engaged in research development activities and 139 are in administrative, business development and sales and marketing positions. We consider relations with our employees to be good. None of our employees are represented by a labor union.

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ITEM 1A. RISK FACTORS

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 and our financial condition and results of operations. In this event, 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 which may never be successfully commercialized.

To date, we have expended significant time, resources, and effort on the development of Oxtellar XR and Trokendi XR, and a substantial majority of our resources are now focused on the commercial launch in the United States of our approved product, Oxtellar XR, which commenced on February 4, 2013, and preparing for the commercial launch of our tentatively approved product, Trokendi XR, which we anticipate to occur in the third quarter of 2013. All of our other product candidates are in earlier stages of development and subject to the risks of failure inherent in developing drug products. Accordingly, our ability to generate significant product revenues in the near term will depend almost entirely on our ability to successfully commercialize Oxtellar XR and our ability to successfully obtain final marketing approval for and commercialize Trokendi XR. We may not sell Trokendi XR in the United States until the FDA grants final marketing approval and, therefore, our planned commercial launch of Trokendi XR in the United States could experience unanticipated delays or problems and may be prohibited altogether, notwithstanding its tentative approval by the FDA.

Our ability to successfully commercialize Oxtellar XR and Trokendi XR will depend on, among other things, our ability to:

maintain commercial manufacturing arrangements with third-party manufacturers for Oxtellar XR and Trokendi XR;

produce, through a validated process, sufficiently large quantities and inventory of our products to permit successful commercialization;

build and maintain a wide variety of internal sales, distribution and marketing capabilities sufficient to build commercial sales of our products;

establish collaborations with third parties for the commercialization of our products in countries outside the United States, and such collaborators' ability to obtain regulatory and reimbursement approvals in such countries;

secure widespread acceptance of our products from physicians, health care payors, patients and the medical community;

properly price and obtain adequate coverage and reimbursement of the product 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; and

manage our growth and spending as costs and expenses increase due to commercialization.

There are no guarantees that we will be successful in completing these tasks. Successful commercialization will also depend on whether we can adequately protect against and effectively

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respond to any claims by holders of patents and other intellectual property rights that our products infringe their rights, whether any unanticipated adverse effects or unfavorable publicity develops in respect of our products, as well as the emergence of new or existing products as competition, which may be proven to be more clinically effective and cost-effective. If we are unable to successfully complete these tasks, we may not be able to commercialize Trokendi XR in a timely manner, or at all, in which case we may be unable to generate sufficient revenues to sustain and grow our business.

In addition, we have begun, and will need to continue, investing substantial financial and management resources to build out our commercial infrastructure and to recruit and train sufficient additional qualified marketing, sales and other personnel in support of our commercial launch of Oxtellar XR and preparation for the commercial launch of Trokendi XR. We have committed and will commit these additional resources prior to obtaining final approval of Trokendi XR from the FDA. If we are unable to successfully obtain final FDA approval of Trokendi XR or complete these activities, or experience unanticipated delays or problems, our costs could substantially increase and our business, financial condition and results of operations will be adversely affected. In addition, we have certain revenue expectations with respect to the sale of Oxtellar XR and Trokendi XR. If we cannot successfully commercialize and achieve those revenue expectations with respect to Oxtellar XR and Trokendi XR, this would result in a material adverse impact on our anticipated revenues and liquidity.

Moreover, even as we launch Oxtellar XR and if we are able to timely launch Trokendi XR, their continued commercial success will be largely dependent on the ability of third-party manufacturers and collaborators. They may not deploy the resources we would like them to, and our revenue would then suffer. In addition, we could become embroiled in disputes with these parties regarding the terms of any agreements, their performance or intellectual property rights. Any dispute could disrupt the sales of our products and adversely affect our reputation and revenue. In addition, if any of our manufacturing or collaboration partners fail to effectively perform under our arrangements for any reason, we may not be able to find a suitable replacement partner on a timely basis, or at all, or on acceptable terms.

Adoption of Oxtellar XR or Trokendi XR may be slow or limited for a variety of reasons including competing branded and generic therapies or safety issues. If either Oxtellar XR or Trokendi XR is not successful in gaining broad commercial acceptance, our business would be harmed.

The rate of adoption of Oxtellar XR and, if approved by the FDA, Trokendi XR will be dependent on several factors including our ability to educate and increase physician awareness of the benefits and cost-effectiveness of our products relative to competing therapies. The degree of market acceptance of any of our 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 and severity of any adverse side effects;

availability of alternative treatments;

pricing and cost effectiveness;

the effectiveness of our sales and marketing capability and strategies; and

ability to obtain sufficient third-party coverage or reimbursement.

In addition, Oxtellar XR and, if approved by the FDA, Trokendi XR will be subject to continual review by the FDA, and we cannot assure you that newly discovered or developed safety issues will not arise. With the use of any newly marketed drug by a wider patient population, serious AEs may occur from time to time that initially do not appear to relate to the drug itself. Any safety issues could cause us to

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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 have rapidly expanded our operations to support the commercial launch of Oxtellar XR and will continue to do so to support increased commercialization of Oxtellar XR and, if approved by the FDA, Trokendi XR, which has significantly increased our costs, and until we achieve economies of scale, we will incur negative margins on sales of Oxtellar XR and Trokendi XR.

We have and expect to continue to significantly increase our investment in commercial infrastructure. We will need to effectively manage the expansion of our operations and facilities and continue to grow our infrastructure to commercialize Oxtellar XR and, if approved by the FDA, Trokendi XR. We must effectively manage our supply chain and distribution network, all of which requires strict planning in order to meet production timelines. In addition to the 75 salespeople we hired to launch Oxtellar XR, we continue to add marketing and sales personnel, and personnel in all other areas of our operations, which strains our existing managerial, operational, financial and other resources. As a result of the scaling of our commercial operations, we expect to incur negative margins on any sales of Oxtellar XR and, if approved by the FDA, Trokendi XR until we are able to generate significant sales volume. We will also need to maintain our commercial manufacturing arrangements with third parties for any approved product to avoid the loss of revenue from potential sales of such product, and adversely impact its market acceptance. If we fail to manage the growth in our systems and personnel appropriately and successfully in order to achieve our commercialization plans for Oxtellar XR and Trokendi XR, our revenues could suffer and our business could be harmed.

We are dependent on the success of our product candidates, which may never receive regulatory approval or be successfully commercialized.

To date, we have expended significant time, resources, and effort on the development of our product candidates, and a substantial majority of our resources are now focused on the commercialization of Oxtellar XR, and planning for the commercialization of our tentatively approved product, Trokendi XR, in the United States. All of our other product candidates are in earlier stages of development and subject to the risks of failure inherent in developing drug products. Accordingly, our ability to generate significant product revenues in the near term will depend almost entirely on our ability to successfully commercialize Oxtellar XR and our ability to successfully obtain final marketing approval for and commercialize Trokendi XR. Trokendi XR has received tentative approval from the FDA and may never be commercialized until we receive final marketing approval from the FDA.

Our ability to successfully commercialize any of our products candidates will depend on, among other things, our ability to:

receive marketing approvals from the FDA and similar foreign regulatory authorities;

produce, through a validated process, sufficiently large quantities of our product candidates to permit successful commercialization;

establish commercial manufacturing arrangements with third-party manufacturers;

build and maintain strong sales, distribution and marketing capabilities sufficient to launch commercial sales of our product candidates;

establish collaborations with third parties for the commercialization of our product candidates in countries outside the United States, and such collaborators' ability to obtain regulatory and reimbursement approvals in such countries;

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secure acceptance of our product candidates from physicians, health care payors, pharmacies, wholesalers, patients and the medical community;

successfully complete our clinical trials; and

manage our spending as costs and expenses increase due to commercialization and clinical trials.

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 Oxtellar XR, Trokendi XR or any of our other product candidates in a timely manner, or at all, in which case we may be unable to generate sufficient revenues to sustain and grow our business. In addition, if we experience unanticipated delays or problems, development costs could substantially increase and our business, financial condition and results of operations will be adversely affected.

We have limited sales and marketing experience and resources, and we may not be able to effectively market and sell our products or product candidates, if approved, in the United States.

We have built our sales and marketing capabilities in the United States to launch Oxtellar XR and, assuming receipt of final approval from the FDA, Trokendi XR. Additionally, there are plans to further expand our sales and marketing capabilities later this year. We have limited sales and marketing experience and have been building such capabilities by investing significant amounts of financial and management resources. We have committed and will commit additional resources to develop internal sales and marketing capabilities prior to any confirmation that Trokendi XR has received final approval from the FDA or any other of our product candidates have been approved by the FDA. We believe that net proceeds from the November 2012 stock offering, together with cash on hand, will be sufficient to fund the commercialization of Oxtellar XR, and complete development and fund the expected commercialization of Trokendi XR if approved by the FDA. We commenced the commercial launch of Oxtellar XR in February 2013 and anticipate the commercial launch of Trokendi XR to occur during the third quarter of 2013 assuming the receipt of final approval by the FDA. If final FDA approval or the commercial launch of Trokendi XR is delayed for any reason, we could incur significant additional expenses prior to being able to realize any revenues. Further, we could face a number of additional risks in establishing internal sales and marketing capabilities, including:

we may not be able to attract talented and qualified personnel to build an effective marketing or sales force capability;

the cost of establishing a marketing and sales force capability may not be justifiable in light of the revenues generated by Oxtellar XR, Trokendi XR if it receives final approval, or any of our product candidates if approved by the FDA; and

our direct sales and marketing efforts may not be successful.

If we are unable to establish adequate sales and marketing capabilities or are unable to do so in a timely manner, we may not be able to generate product revenues and may never become profitable.

The commercial success of our products and product candidates, if approved, depends upon attaining market acceptance by physicians, patients, third-party payors and the medical community.

Physicians may not prescribe Oxtellar XR, Trokendi XR, if approved by the FDA, or any of our product candidates if approved by the FDA, in which case we would not generate the revenues we anticipate. Market acceptance of any of our products or product candidates by physicians, patients, third-party payors and the medical community depends on, among other things:

our ability to provide acceptable evidence of safety and efficacy;

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acceptance by physicians and patients of each product or product candidate as a safe and effective treatment;

perceived advantages of our products or product candidates over alternative treatments;

relative convenience and ease of administration of our products or product candidates compared to existing treatments;

any labeling restrictions placed upon each product or product candidate in connection with its approval;

the prevalence and severity of the adverse side effects of each of our products or product candidates;

the clinical indications for which each of our products or product candidates are approved, including any potential additional restrictions placed upon each product or product candidate in connection with its approval;

prevalence of the disease or condition for which each product or product candidate is approved;

the cost of treatment in relation to alternative treatments, including generic products;

the extent to which each product or product candidate is approved for inclusion on formularies of hospitals and managed care organizations;

any negative publicity related to our or our competitors' products or product candidates, including as a result of any related adverse side effects;

the effectiveness of our or any current or future collaborators' sales, marketing and distribution strategies;

pricing and cost effectiveness; and

the availability of adequate reimbursement by third parties.

For example, new AEDs that were introduced in the market as NCEs historically have not quickly gained significant market share against existing molecules in the epilepsy market, because physicians are often reluctant to change a stable patient's existing therapy (even for an NCE) and risk a breakthrough seizure or tolerability issues in their patients. Although Oxtellar XR and, if commercially launched, Trokendi XR, are not NCEs, they would be subject to the risk that they will not be able to gain significant market share against existing AEDs. If our products or product candidates do not achieve an adequate level of acceptance by physicians, third-party payors and patients, we may not generate sufficient revenues from these products or product candidates to become or remain profitable on a timely basis, if at all.

Final marketing approval of Trokendi XR, or any of our product candidates 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 products and product candidates. We are not permitted to market any of our product candidates in the United States until we receive approval of an NDA from the FDA, or in any foreign jurisdiction until we receive the requisite approvals from such jurisdiction. 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, if any.

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With respect to Trokendi XR, we submitted an NDA under Section 505(b)(2) of the FDCA, which allows us to rely in our submissions on the existing data from the NDA of Topamax. Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments, and 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 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 or clinical trials demonstrating safety and effectiveness. The FDA could refuse to approve our current NDA submission, or require additional information to sufficiently demonstrate safety and effectiveness. For example, we initially submitted an NDA for Trokendi XR in January 2011, but the FDA refused to file the NDA and raised questions relating to chemistry and manufacturing control issues. Although, the FDA accepted the NDA for filing in November 2011, it granted only tentative approval for Trokendi XR in June 2012 citing the need for inclusion on the product's label of certain pediatric safety information of the reference listed drug Topamax, which is the subject of marketing exclusivity until June 2013. There can be no assurance that the FDA will grant final approval of our NDA when this marketing exclusivity expires or at any time thereafter.

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

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 United States, 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;

may determine that we have identified the wrong reference listed drug or drugs or that approval of our Section 505(b)(2) application for Trokendi XR, or any of our other product candidates, 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 the API used in our product candidates;

may identify deficiencies in the manufacturing processes or facilities of third-party manufacturers with which we enter into agreements for the manufacturing of our product candidates;

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.

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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

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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.

Our trials may fail to demonstrate acceptable levels of safety, efficacy or any other requirements of our product candidates, 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 FDA with respect to approval in the United States (and to the satisfaction of similar regulatory authorities in other jurisdictions with respect to approval in those jurisdictions), that each product candidate is safe and effective for use in the target indication. The FDA may require us 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 and, ultimately, the commercialization of that product candidate.

In addition, the results from the trials that we have completed for our product candidates may not be replicated in future trials, or we may be unable to demonstrate sufficient safety and efficacy to obtain the requisite regulatory approvals for our product candidates. 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 could be delayed or might be terminated.

Our products and product candidates may cause undesirable side effects or have other properties that limit their commercial potential or 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 potential products liability claims. Any undesirable side effects that are caused by any of our product candidates could have a material adverse effect upon that product candidate's development program and our business as a whole.

Immediate release oxcarbazepine and topiramate, drug compounds upon which Oxtellar XR and Trokendi XR are based, respectively, are known to cause various side effects, including dizziness, paresthesia, headaches, cognitive deficiencies such as memory loss and speech impediment, digestive problems, somnolence, double vision, gingival enlargement, nausea, weight gain, 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.

If these 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 the product candidate, a number of potentially significant negative consequences could result, including:

regulatory authorities may withdraw approvals 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 risks of such side effects for distribution to patients;

we may be required to modify the product in some way;

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the FDA 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; and

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.

If other versions of extended or controlled release oxcarbazepine or topiramate are approved and successfully commercialized, especially if an extended or controlled release topiramate anti-epileptic drug is approved before Trokendi XR receives final approval, our business would be materially harmed.

Other third parties may seek approval to manufacture and market their own versions of extended release oxcarbazepine or topiramate anti-epileptic drugs in the United States. If any of these parties obtain FDA approval of an extended release topiramate product before we do, they may be entitled to three years of marketing exclusivity. Such exclusivity would, for example, delay the commercialization of Trokendi XR and, as a result, we may never achieve significant market share for this tentatively approved product. Consequently, revenues from product sales of these products would be similarly delayed and our business, including our development programs, and growth prospects would suffer. For example, we are aware that Upsher-Smith's USL255 (extended release topiramate) is in Phase III clinical development for the treatment of epilepsy in adults and its NDA may have been filed or is being prepared for filing. If Upsher-Smith's USL255 product is approved by the FDA before Trokendi XR, then Upsher-Smith may obtain three years of marketing exclusivity based on its Phase III clinical trial, which would significantly delay our entry into the U.S. market. Even if Trokendi XR is approved before USL255, we may not be entitled to any marketing exclusivity and, other than under circumstances in which third parties may infringe or are infringing our patents, we may not be able to prevent the submission or approval of another full NDA for any competitor's extended or controlled release topiramate product candidate, including USL255. In addition, we are aware of companies who are marketing modified-release oxcarbazepine products outside of the United States, such as Apydan, which is developed by Desitin Arzneimittel GmbH and requires twice-daily administration. If companies with modified-release oxcarbazepine products outside of the United States pursue or obtain approval of their products within the United States, such competing products may limit the potential success of Oxtellar XR in the United States, and our business and growth prospects would be materially impaired. Accordingly, if any third party is successful in obtaining approval to manufacture and market their own versions of extended release oxcarbazepine or topiramate in the United States, we may not be able to recover expenses incurred in connection with the development of or 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 supplemental NDAs, including Section 505(b)(2) applications, for, among other things, new indications, dosage forms, routes of administration, or strengths of an existing drug, or for a new use, if 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, which is 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 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

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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 active 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 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. While the FDA granted a three year marketing exclusivity period for Oxtellar XR, the FDA has not yet determined whether it will grant marketing exclusivity for Trokendi XR and we cannot assure you that we will receive any such marketing exclusivity from the FDA for Trokendi XR or any of our product candidates. If we are unable to obtain marketing exclusivity for our products or product candidates, then our competitors may obtain approval of competing products more easily than if we had such marketing exclusivity, and our future revenues could be reduced, possibly materially.

Delays or failures in the completion of testing 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 obtaining regulatory approval to commence a clinical trial or 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 organizations, or CROs, and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

insufficient or inadequate supply or quantity of a product candidate for use in trials;

difficulties obtaining 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 initiated a clinical trial but may be prone to withdraw due to side effects from the therapy, lack of efficacy or personal issues; and

clinical holds imposed by the FDA.

Clinical trials may also be delayed as a result of ambiguous or negative interim results. In addition, clinical trials may be suspended or terminated by us, an IRB or ethics committee overseeing the clinical trial at a trial site (with respect to that site), 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 clinical hold;

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unforeseen safety issues; or

lack of adequate funding to continue the trial.

In addition, failure to conduct the clinical trial in accordance with regulatory requirements or the trial protocols may also result in the inability to use the data to support product approval. For instance, the efficacy demonstrated by SPN-810 in its most recent Phase IIb study was not statistically significant for all efficacy measures for the study. Additionally, changes in regulatory requirements and guidance may occur, and we may need to amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to institutional review boards or ethics committees for reexamination, which may impact the costs, timing 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 will be diminished.

We expect intense competition and, if our competitors develop or market alternatives for treatments 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 competing products will limit the demand and the price we are able to charge for any of our products or product candidates that are commercialized unless we are able to differentiate them. We anticipate that we will face intense competition when our product candidates are approved by regulatory authorities and we begin the commercialization process for our products. For instance, there are over 15 branded products, as well as their generic counterparts, on the U.S. market indicated to treat epilepsy. In addition, several NCEs have entered the epilepsy market including Potiga, Vimpat and Banzel. Another NCE, Stedesa, could be approved later in 2013 and enter the market thereafter. In addition, competition in the ADHD market in the United States 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. As a result, we may not be able to recover expenses incurred in connection with the development of our product candidates or realize revenues from any commercialized product.

In addition to already marketed competing products, we believe certain companies are developing other products which could compete with our product candidates should they be approved by regulatory authorities. For example, according to Datamonitor, as of April 2010, there were 47 compounds in preclinical and clinical development for epilepsy across the United States, Japan, France, Germany, Italy, Spain and the United Kingdom. Datamonitor reported that approximately 13 were in late-stage (Phase II or later) clinical trials as of June 2011. We are also aware that Upsher-Smith's USL255 (extended release topiramate) is in Phase III clinical development for the treatment of epilepsy in adults and its NDA may have been filed or is being prepared for filing. If successful, such competing product could limit the potential success of Trokendi XR, and our growth prospects would be materially impaired. In addition, we are aware of companies who are marketing outside of the United States modified-release oxcarbazepine products, such as Apydan, which is developed by Desitin Arzneimittel GmbH and requires twice-daily administration. We are also aware that Qsymia, an oral drug containing ER topiramate and another API, is available in extended release for treatment of weight management. If companies with modified-release oxcarbazepine products outside of the United States obtain approval for their products within the United States, then such competing products may limit the potential success of Oxtellar XR. Further, new developments, including the development of

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other drug technologies, may render our 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 any commercialized product.

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;

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 product candidates that are approved, our business, results of operations, financial condition and prospects may be materially 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, if they receive regulatory approval, may be subject to restrictions or withdrawal from the market and we may be subject to penalties if we fail to comply with regulatory requirements.

Even if U.S. regulatory approval is obtained, the FDA may still impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies. 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 post-market 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 cGMP regulations. If we, our collaborators or a regulatory authority discovers previously unknown problems with a product, such as side effects of unanticipated 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. 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;

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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; or

seize or detain products or require us to initiate a product recall.

In addition, our product labeling, advertising and promotion of our approved product, and our tentatively approved product and our product candidates upon FDA approval, 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. Physicians may nevertheless prescribe our products and, upon receiving FDA approval, our product candidates to their patients in a manner that is inconsistent with the approved label. 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 improperly 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, if any.

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.

We do not currently 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 to develop our own manufacturing operations for Phase III clinical materials or commercial products in the foreseeable future. We currently depend on third-party contract manufacturers for the supply of the APIs for our products or product candidates, including drug substance for our preclinical research and clinical trials. For Oxtellar XR and Trokendi XR, we currently rely on single suppliers for raw materials including API and single manufacturers 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 effects on us. 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.

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, including stability of the product and quality assurance testing, 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 obtain FDA approval and market our products and product candidates would be jeopardized. In addition, any delay or interruption in the supply of clinical trial supplies could delay or prohibit the completion of our bioequivalence and/or clinical trials, increase the costs associated with conducting our bioequivalence

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and/or 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 enforced by the FDA through their facilities inspection programs. These requirements include, among other things, 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 or product candidates, and we may be held liable for any injuries sustained as a result. Any of these factors could cause a delay in clinical developments, regulatory submissions, approvals or commercialization of our products or 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 or product candidates, and would lose potential revenues.

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, in turn, be cited by potential competitors in support of approval of an ANDA. 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. 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 candidate and that the generic product is bioequivalent to ours, meaning it is absorbed in the body at the same rate and to the same extent as our 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 and companies that produce generic equivalents are generally able to offer their products at lower prices. Thus, after the introduction of a generic competitor, a significant percentage of the sales of any branded product is typically lost to the generic product. Accordingly, competition from generic equivalents to our product candidates would materially adversely impact our revenues, profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made in our product candidates.

We intend to rely on third-party collaborators to market and commercialize our product candidates outside of the United States, who may fail to effectively commercialize our product candidates.

Outside of the United States, we currently plan to utilize strategic partners or contract sales forces, where appropriate, to assist in the commercialization of our product candidates, if approved. We currently possess limited resources and may not be successful in establishing collaborations or co-promotion arrangements on acceptable terms, if at all. We also face competition in our search for collaborators and co-promoters. By entering into strategic collaborations or similar arrangements, we will rely on third parties for financial resources and for development, commercialization, sales and marketing and regulatory expertise. Our collaborators may fail to develop or effectively commercialize our 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

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third-party collaborators to successfully market and commercialize our product candidates outside of the United States 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.

Our success will depend on our ability to obtain and maintain patent protection for our proprietary technologies and our 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 United States and internationally for our product candidates. Our policy is to actively seek to protect our proprietary position by, among other things, filing patent applications in the United States 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 be uncertain. Patent applications in the United States 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 United States, 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 will be costly and time consuming, and an unfavorable outcome in that litigation would 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 their approved products and our product candidates and 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 industry expands and more patents are issued, the risk increases that our collaborators' approved products and 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, Trokendi XR or any of our product

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candidates, which could prevent us from being able to commercialize Oxtellar XR, Trokendi XR or any of our product candidates, respectively. Because patent applications can take many years to issue, there may be currently pending applications which may later result in issued patents that our collaborators' approved 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 or our products or 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 and could be unable to commercialize the applicable approved products and 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, pending a trial on the merits, which 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 or violates the third party's rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages and the patent owner's attorneys' fees;

a court prohibiting us from selling Oxtellar XR, Trokendi XR, or any product candidate approved in the future, if any, 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 Oxtellar XR, Trokendi XR, or any of our product candidates so they do not infringe, which may not be possible or may require substantial monetary expenditures and time.

We may become 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 are involved in the following matters related to Paragraph IV Certification Notice Letters that we have received in connection with our collaborators' products. In connection with an ANDA, a Paragraph IV Certification Notice Letter notifies the FDA that one or more patents listed in the FDA's Approved Drug Product List (Orange Book) is alleged to be invalid, unenforceable or will not be infringed by the ANDA product.

Sanctura XR Litigation. We are involved in a patent infringement matter filed in response to three Paragraph IV Certification Notice Letters that we received in June 2009, November 2009 and April 2010 regarding an ANDA submitted to the FDA by each of Watson Laboratories, Inc., Sandoz Inc. and Paddock Laboratories, Inc., respectively, requesting approval to market and sell generic versions of Sanctura XR trospium chloride extended release capsules, a product that is manufactured and sold by Allergan, Inc., which is the marketing partner of Endo

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Pharmaceuticals Solutions Inc. The ANDA filers alleged in their respective original notice letters that U.S. Patent Number 7,410,978 issued to us is invalid, unenforceable and/or will not be infringed by the respective company's manufacture, use or sale of the product described in its ANDA submission. Our patent covers extended-release formulations containing trospium chloride and expires on February 1, 2025, and is licensed to Endo Pharmaceuticals Solutions Inc. Each of the ANDA filers subsequently amended their respective notice letters to include other U.S. patents related to Sanctura XR trospium chloride (specifically, U.S. Patent Nos. 7,759,359; 7,763,635; 7,781,448; and 7,781,449). In March 2012, the court ruled that the defendants' proposed products infringe the patents-in-suit and that the patents-in-suit are invalid. Allergan, Inc. and Endo Pharmaceuticals Solutions Inc. filed an appeal, and the Federal Circuit heard argument on June 14, 2012. The Federal Circuit issued a Rule 36 summary affirmance of the District Court's decision that the patents were invalid on June 18, 2012. Allergan, Inc. and Endo Pharmaceuticals Solutions Inc. filed a petition for writ of certiorari on September 17, 2012, which was denied by the U.S. Supreme Court on October 15, 2012, thereby declining to disturb the earlier judicial finding that the patents are invalid. We do not expect the resulting entry of competitive generic products to have a material adverse effect on our current business.

Oracea Litigation. We are involved in a patent infringement case filed in the District of Delaware in response to Paragraph IV Certification Notice Letters that we received in September 2011 and September 2012 regarding an ANDA submitted to the FDA by Amneal Pharmaceuticals LLC, requesting approval to market and sell generic versions of Oracea (30 mg immediate release, 10 mg delayed release doxycycline), a product that is manufactured and sold by Galderma Laboratories, L.P. Amneal alleged its notice letters that U.S. Patent Nos. 7,749,532, or the '532 patent, and 8,206,740, or the '740 patent, which are both assigned to us, are invalid, unenforceable and/or will not be infringed by the manufacture, use or sale of the product described in its ANDA. In addition, in October 2010, we received a complaint for declaratory judgment from Mylan Pharmaceuticals Inc., or Mylan, alleging invalidity of the '532 patent. This case was tried in July 2011 in the District of Delaware. The district court held that Mylan infringed certain claims of the patent, and that the patent claims are valid. This district court decision is currently being appealed by Mylan; Lupin Limited and Lupin Pharmaceuticals, Inc.; and Impax Laboratories, Inc. to the U.S. Court of Appeals for the Federal Circuit. The '532 patent and the '740 patent cover once-daily formulations of doxycycline, including their methods use in treating rosacea and processes regarding their preparation. Both patents expire on December 19, 2027 and are licensed to Galderma Laboratories, L.P. We intend to support Galderma Laboratories, L.P. in these matters. We do not expect an adverse decision in the foregoing matters will have a material adverse effect on our current business.

Intuniv Litigation. We are involved in several patent infringement actions in district courts throughout the United States, which were filed in response to Paragraph IV Certification Notice Letters that we received in March, April and October 2010, and February, March and October 2011, regarding ANDAs submitted to the FDA requesting approval to market and sell generic versions of Intuniv, a product that is manufactured and sold by Shire LLC. The defendants in these cases are Teva Pharmaceuticals USA, Inc. and Teva Pharmaceutical Industries, Ltd; Actavis Elizabeth LLC and Actavis, Inc.; Watson Pharmaceuticals, Inc., Watson Laboratories, Inc. Florida Watson Pharma, Inc. and ANDA, Inc.; Impax Laboratories, Inc.; Sandoz Inc. and Mylan Pharmaceuticals Inc. and Mylan Inc. The ANDA filers allege that our U.S. Patent Nos. 6,287,599 and 6,811,794 are invalid, unenforceable and/or will not be infringed by the manufacture, use or sale of the product described in its ANDA submissions. A bench trial was held on September 17-20, 2012 in the District of Delaware in the case against defendants Teva Pharmaceuticals USA, Inc.; Teva Pharmaceutical Industries, Ltd.; Actavis Elizabeth LLC; and Actavis, Inc. No decision has yet been issued by the district court in that case. Prior to the trial in the District of Delaware, Shire LLC settled all claims against defendants Anchen

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Pharmaceutical, Inc., Anchen Inc. and TWi Pharmaceuticals, Inc. in connection with TWi's ANDA for a generic version of Intuniv. Our patents cover extended-release formulations containing guanfacine hydrochloride, with the latest patent expiration in July 2022. Both of these patents are licensed to Shire LLC. We intend to support Shire LLC in its efforts to contest this matter. We do not expect an adverse decision in the foregoing matter will have a material adverse effect on our current business.

In any infringement proceeding including the foregoing, a court may decide that a patent of ours is not valid or is unenforceable, 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 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. Litigation or interference proceedings may fail and, even if successful, 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, 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, it could have a substantial adverse effect on the price of our common stock. There can be no assurance that our products or product candidates will not be subject to the same risks.

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 to use one of our proprietary technologies for an oral formulation of treprostinil diethanolamine, or treprostinil, for the treatment of PAH, as well as for other indications. This oral formulation was the subject of an NDA for PAH submitted by United Therapeutics and accepted for filing by the FDA in February 2012. On October 23, 2012, United Therapeutics received a complete response letter from the FDA declining to approve the product. Accordingly, we do not expect to receive any royalties for this formulation in this indication unless and until final marketing approval from the FDA is received and until United Therapeutics launches this product. 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, however, we could lose the potential to receive any future royalty payments thereunder, which could be financially significant to us.

We also have license agreements with Especificos Stendhal, S.A., DE C.V. and we may enter into additional collaborations in the future. 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

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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 in these industries. 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;

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

may 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 collaborations with us;

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

may fail to comply with applicable regulatory requirements;

may not be able to obtain the necessary marketing approvals; or

may breach or terminate their arrangement with us.

If collaboration partners fail to develop or effectively commercialize our products or product candidates for any of these reasons, we may not be able to replace the collaboration partner with another partner to develop and commercialize the product or product candidate under the terms of the collaboration. 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, which could adversely affect our results of operations.

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

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

the possible breach of the agreements by the CROs or CMOs because of factors beyond our control or the insolvency of any of these third parties or other financial difficulties, labor unrest, natural disasters or other factors adversely affecting their

ability to conduct their business; and

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termination or non-renewal of an agreement by the third parties, at a time that is costly or inconvenient for us, because of our breach of the manufacturing agreement or based on their own business priorities.

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 to develop our own manufacturing operations for Phase III clinical materials or commercial products in the foreseeable future. We currently depend on third-party CMOs for all of our required raw materials and drug substance for our preclinical research and clinical trials. For Oxtellar XR and Trokendi XR, we currently rely on single suppliers for raw materials, including API, and expect to rely on third-party suppliers and manufacturers for the final commercial products. If any of these vendors is unable to perform its obligations to us, including due to violations of the FDA's requirements, our ability to meet regulatory requirements or projected timelines and necessary quality standards for successful manufacture of the various required lots of material for our development and commercialization efforts would be adversely affected. Further, if we were required to change vendors, it could result in delays in our regulatory approval 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 prospects.

We have entered into supply agreements for both Oxtellar XR and Trokendi XR with leading CMOs headquartered in North America for the manufacture of the final commercial products. However, there is a risk that the counterparties to these agreements will not perform their respective obligations or will terminate these agreements. In addition, we do not have contractual relationships for the manufacture of commercial supplies of all of our product candidates. The number of third-party manufacturers with the expertise, required regulatory approvals and facilities to manufacture drug substance and final drug product on a commercial scale is limited. Therefore, we may not be able to enter into such arrangements with third-party manufacturers in a timely manner, on acceptable terms or at all. Failure to secure such contractual arrangements would harm the commercial prospects for our product candidates, our costs could increase and our ability to generate revenues could be delayed.

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

We are a party to and rely on several arrangements with third parties, such as those with Afecta and Rune, which give us rights to intellectual property that is necessary for the development of certain of our product candidates including SPN-810 and SPN-809, respectively. In addition, we may enter into similar arrangements in the future. Our current arrangements impose various development, royalty and other obligations on us. If we materially breach these obligations or if Afecta or Rune fail to adequately perform their respective obligations, these exclusive arrangements could be terminated, which would result in our inability to develop, manufacture and sell products that are covered by such intellectual property.

Even if our product candidates receive regulatory approval in the United States, we or our collaborators may never receive approval to commercialize our product candidates outside of the United States.

In order to market any products outside of the United States, 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 United States. 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 United States as well as other risks. For example, legislation analogous to

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Section 505(b)(2) of the FDCA in the United States, 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 is 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.

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 other jurisdictions or any delay or setback in obtaining such approvals could have the same adverse effects detailed above regarding FDA approval in the United States. As described above, such effects include the risks that any of our product candidates may not be approved for all indications requested, which could limit the uses of our product candidates and have an adverse effect on their commercial potential or require costly post-marketing studies.

Guidelines and recommendations published by various organizations can reduce the use of our products and product candidates.

Government agencies promulgate regulations and guidelines directly applicable to us and to our products and product candidates. In addition, professional societies, practice management groups, private health and science foundations and organizations involved in various diseases from time to time may also publish guidelines or recommendations to the health care and patient communities. Recommendations of government agencies or these other groups or organizations may relate to such matters as usage, dosage, route of administration and use of concomitant therapies. Recommendations or guidelines suggesting the reduced use of our products or product candidates or the use of competitive or alternative products that are followed by patients and health care providers could result in decreased use of our products or product candidates.

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 and product candidates, including Oxtellar XR and Trokendi XR, 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 have been 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 these 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 AEDs. 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. Reduced or partial payment or 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 discount, which would adversely affect our ability to realize an appropriate return on our investment in our products or product candidates or compete on price.

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. Because each third-party payor individually approves payment or reimbursement, obtaining these approvals can be a time 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

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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, and we may ultimately be unsuccessful in obtaining coverage. Our competitors generally have larger organizations, as well as 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 to a smaller set than we believe they are effective in treating.

In some foreign countries, particularly Canada and the countries of 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 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.

In addition, many managed care organizations negotiate the price of products and develop 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 adequate payment or reimbursement levels are not provided, or if those policies increasingly favor generic products, our market share and gross margins could be negatively affected, which would have a material adverse effect on our overall business and financial condition.

We expect to experience pricing pressures due to the potential healthcare reforms discussed elsewhere in this Annual Report on Form 10-K, as well as the trend toward programs aimed at reducing health care costs and the increasing influence of health maintenance organizations and additional legislative proposals.

We face potential product liability exposure, and, if successful claims are brought against us, we may incur substantial liabilities.

The use of our product candidates in clinical trials and the sale of any of our products expose us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers or others selling or otherwise coming into contact with our products and product candidates. If we cannot successfully defend ourselves against product liability claims, we could incur substantial liabilities. In addition, product liability claims may result in:

decreased demand for any product or product candidate that has received approval and is being commercialized;

impairment of our business reputation and exposure to adverse publicity;

withdrawal of bioequivalence and/or clinical trial participants;

initiation of investigations by regulators;

costs of related litigation;

distraction of management's attention from our primary business;

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substantial monetary awards to patients or other claimants;

loss of revenues; and

the inability to commercialize any of our product candidates for which we obtain marketing approval.

Our product liability insurance coverage for our clinical trials is limited to \$10 million per claim and \$10 million in the aggregate, and covers bodily injury and property damage arising from our clinical trials, subject to industry-standard terms, conditions and exclusions. Our insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses. We have expanded our insurance coverage to include the sale of commercial products prior to the commercialization of our products. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

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

As part of our growth strategy, we intend to develop and market additional product candidates. We are pursuing various therapeutic opportunities through our pipeline. We may spend several years completing our development of any particular current or future internal product candidate, and failure can occur at any stage. The product candidates to which we allocate our resources may not end up being 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 products.

The process of proposing, negotiating and implementing a license or acquisition of 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 acquisition of product candidates and approved products. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses and technologies and integrate them into our current infrastructure. Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, 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;

incurrence of substantial debt, dilutive issuances of securities or depletion of cash to pay for acquisitions;

higher than expected acquisition and integration costs;

difficulty in combining the operations and personnel of any acquired businesses with our operations and personnel;

increased amortization expenses;

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impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and

inability to motivate key employees of any acquired businesses.

Further, any product candidate that we acquire may require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the FDA 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.

Healthcare reform measures could hinder or prevent our product candidates' commercial success.

The U.S. government and other governments have shown significant interest in pursuing healthcare reform. Government-adopted reform measures could adversely impact the pricing of healthcare products and services in the United States or internationally and the amount of reimbursement available from governmental agencies or other third-party payors. The continuing efforts of the U.S. and foreign governments, insurance companies, managed care organizations and other payors of health care services to contain or reduce healthcare costs may adversely affect our ability to set prices for any approved product candidate which we believe are fair, and our ability to generate revenues and achieve and maintain profitability.

In both the United States and some foreign jurisdictions, there have been a number of legislative and regulatory proposals and initiatives to change the health care system in ways that could affect our ability to sell any approved product profitably. Some of these proposed and implemented reforms could result in reduced reimbursement rates for our products, which would adversely affect our business strategy, operations and financial results. For example, in March 2010, President Obama signed into law a legislative overhaul of the U.S. healthcare system, known as the Patient Protection and Affordable Care Act of 2010, as amended by the Healthcare and Education Affordability Reconciliation Act of 2010. These laws and their regulations, which we refer to collectively as the Health Care Reform Law, may have far reaching consequences for biopharmaceutical companies like us. As a result of the Healthcare Reform Law, substantial changes could be made to the current system for paying for healthcare in the United States, including changes made in order to extend benefits to those who currently lack insurance coverage or changing coverage parameters. Extending coverage to a large population could substantially change the structure of the health insurance system and the methodology for reimbursing medical services and drugs. These structural changes could entail modifications to the existing system of private payors and government programs, such as Medicare and Medicaid, creation of a government-sponsored healthcare insurance source, or some combination of both, as well as other changes. Restructuring the coverage of medical care in the United States could impact the reimbursement for prescribed drugs, including our products and product candidates. If reimbursement for our approved products is substantially less than we expect in the future, or rebate obligations associated with them are substantially increased, our business could be materially and adversely impacted.

In September 2007, the Food and Drug Administration Amendments Act of 2007 was enacted, giving the FDA enhanced post-marketing authority, including the authority to require post-marketing studies and clinical trials, labeling changes based on new safety information, and compliance with risk evaluations and mitigation strategies approved by the FDA. In July 2012, the Food and Drug Administration Safety and Innovation Act was enacted, expanding drug supply chain requirements and strengthening FDA's response to drug shortages, among other things. The FDA's exercise of this authority could result in delays or increased costs during product development, clinical trials and regulatory review, increased costs to assure compliance with post-approval regulatory requirements, and potential restrictions on the sale and/or distribution of any approved product candidates.

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Future federal and state proposals and health care reforms could limit the prices that can be charged for the product candidates that we develop and may further limit our commercial opportunity. Our results of operations could be materially adversely affected by the Health Care Reform Law by reducing the amounts that private insurers will pay and by other health care reforms that may be enacted or adopted in the future.

We will need to increase the size of our organization, and we may experience difficulties in managing growth.

We will need to manage our anticipated growth and increased operational activity. Our personnel, systems and facilities currently in place may not be adequate to support this future growth. Our future financial performance and our ability to compete effectively will depend, in part, on our ability to effectively manage any future growth. Our need to effectively execute our growth strategy requires that we:

manage our regulatory approvals and clinical trials effectively;

manage our internal development efforts effectively while complying with our contractual obligations to licensors, licensees, contractors, collaborators and other third parties;

develop internal sales and marketing capabilities;

commercialize our product candidates;

improve our operational, financial and management controls, reporting systems and procedures; and

attract and motivate sufficient numbers of talented employees.

This future growth could place a strain on our administrative and operational infrastructure and may require our management to divert a disproportionate amount of its attention away from our day-to-day activities. We may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. We may not be able to make improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls. If our management is unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate or increase our revenues could be reduced and we may not be able to implement our business strategy.

We may not be able to manage our business effectively if we are unable to attract, motivate and retain key members of our current management team.

We may not be able to attract or motivate qualified management and 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 will significantly impede the achievement of our objectives.

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. We do not have any employment agreements with any member of our senior management team except Mr. Khattar. 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 and generate concern among employees and those with whom we do business.

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In addition to the competition for personnel, our corporate officers 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.

We also have scientific and clinical advisors who assist us in formulating our product development and clinical strategies. These advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us, or may have arrangements with other companies to assist in the development of products that may compete with ours.

If we fail to comply with healthcare regulations, we could face substantial penalties and our business, operations and financial condition could be adversely affected.

As a supplier of pharmaceuticals, certain federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. We could be subject to healthcare fraud and abuse and patient privacy regulation by both the federal government and the states in which we conduct our business. The regulations include:

the federal healthcare program anti-kickback law, which prohibits, among other things, persons from soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs;

federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent, and which may apply to entities like us which provide coding and billing advice to customers;

the federal Health Insurance Portability and Accountability Act of 1996, which prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters and which also imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information;

the federal transparency requirements under the Health Care Reform Law requires manufacturers of drugs, devices, biologics, and medical supplies to report to the Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests;

the FDCA, which among other things, strictly regulates drug product marketing, prohibits manufacturers from marketing drug products for off-label use and regulates the distribution of drug samples; and

state law equivalents of each of the above federal laws, such as anti-kickback, Sunshine Act, and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by federal laws, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations could be costly. If our operations are found to be in violation of any of the laws described above or any governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could

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adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

Our business involves the use of hazardous materials, and we must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our activities and our third-party manufacturers' and suppliers' activities involve the controlled storage, use and disposal of hazardous materials owned by us. We and our manufacturers and suppliers are subject to federal, state, city and local laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. Although we believe that the safety procedures we use for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials. In the event of an accident, local, city, state or federal authorities may curtail the use of these materials and interrupt our business operations, including our commercialization and research and development efforts. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources. We do not currently maintain biological or hazardous materials insurance coverage.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

We employ individuals who were previously employed at other pharmaceutical companies, including our competitors or potential competitors and, as such, we may be subject to claims that we or these employees have used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

Our business and operations would suffer in the event of system failures.

Despite the implementation of security measures, our internal computer systems and those of our contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such an event could cause interruption of our operations. For example, the loss of data from completed or ongoing bioequivalence and/or clinical trials for our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs. To the extent that any disruption or security breach

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was to result in a loss of or damage to our data, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the development of our product candidates could be delayed.

We will need to obtain FDA approval of any proposed product names, and any failure or delay associated with such approval may adversely impact our business.

Any name we intend to use for our product candidates will require approval from the FDA regardless of whether we have secured a formal trademark registration from the USPTO. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. The FDA may object to any product name we submit if it believes the name inappropriately implies medical claims. We have in the past been required to change a proposed product name. If the FDA objects to any of our proposed product names, we may be required to adopt an alternative name for our product candidates. If we adopt an alternative name, we would lose the benefit of our existing trademark applications for such product candidate, and may be required to expend significant additional resources in an effort to identify a suitable product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. We may be unable to build a successful brand identity for a new trademark in a timely manner or at all, which would limit our ability to commercialize our product candidates.

Provisions in our agreement with Shire impose restrictive covenants on us, which could limit our ability to operate effectively in the future.

In 2005, we purchased substantially all of the assets of Shire Laboratories Inc. Pursuant to this agreement, we agreed to refrain perpetually from engaging in any research, formulation development, analytical testing, manufacture, technology assessment or oral bioavailability screening that relate to five specific drug compounds (amphetamine, carbamazepine, guanfacine, lanthanum and mesalamine) and any derivative thereof. Although these various restrictions and covenants on us do not currently impact our product candidates or business, they could in the future limit or delay our ability to take advantage of business opportunities that may relate to such compounds.

Risks Related to Our Finances and Capital Requirements

We have incurred significant operating losses since our inception and anticipate that we will incur continued losses for the foreseeable future.

In recent years, we have focused primarily on developing our current products and product candidates, with the goal of commercializing these products and supporting regulatory approval for these product candidates. We have financed our operations primarily through private placements of convertible preferred stock, our collaboration and license arrangements, the monetization of certain future royalty streams under our existing licenses for Oracea, Sanctura XR and Intuniv, the sale of our subsidiary, Royalty Sub, which held the license rights to Oracea and Sanctura XR, borrowing via secured loans and the completion of our initial public offering in May 2012 and a follow-on offering in November 2012. We have incurred significant operating losses since our inception in 2005. We incurred net losses of approximately \$33.5 million, \$38.5 million and \$46.3 million in the years ended December 31, 2008, 2010 and 2012, respectively. We realized net income of approximately \$0.5 million and \$53.8 million in the years ended December 31, 2009 and 2011, respectively, due to one-time items. As of December 31, 2012, we had an accumulated deficit of approximately \$86.3 million. Substantially all of our operating losses resulted from costs incurred in connection with our development programs and from selling, general and administrative costs associated with our operations. For example, the expenses that we have incurred relating to the research and development of Oxtellar XR and Trokendi XR from inception to December 31, 2012 are approximately \$53.3 million and \$32.5 million, respectively. We expect our research and development costs to continue to be substantial and to increase with respect to

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our product candidates as we advance those product candidates through preclinical studies, clinical trials, manufacturing scale-up and other pre-approval activities. We expect to incur significant and increasing marketing and selling costs prior to and during the commercial launch of our current products. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when, or if, we will become profitable.

Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. Furthermore, since the completion of our initial public offering in May 2012, we have incurred additional costs associated with operating as a public company. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. In this regard, the report of our independent registered public accounting firm with respect to our consolidated financial statements as of and for the period ended December 31, 2012 contains an explanatory paragraph stating that there is substantial doubt about our ability to continue as a going concern. While we believe that the proceeds of the follow-on offering, together with our cash, cash equivalents and marketable securities and anticipated future product revenues will be sufficient to fund the commercialization of Oxtellar XR and, if we receive final approval by the FDA, Trokendi XR, there can be no assurance that we will be able to obtain the additional capital that we anticipate needing in order to become cash flow positive. In addition, we may need to obtain additional funds to develop and commercialize our other product candidates. The inclusion of a going concern statement by our auditors, our lack of cash resources and our potential inability to continue as a going concern may materially adversely affect our share price and our ability to raise new capital or to enter into critical contractual relations with third parties.

We may need additional funding and may be unable to raise capital when needed, which would force us to delay, reduce or eliminate our product development programs or commercialization efforts.

Developing product candidates, conducting clinical trials, establishing manufacturing relationships and marketing drugs are expensive and uncertain processes. Although we believe the proceeds of the November 2012 public offering, together with our cash, cash equivalents and marketable securities and anticipated future product revenues, will be sufficient to allow us to fund the commercialization of Oxtellar XR, and, assuming receipt of FDA approval, Trokendi XR, we will need to obtain additional capital through equity offerings, debt financing, payments under new or existing licensing and research and development collaboration agreements, or any combination thereof, in order to become cash flow positive and to develop and commercialize additional product candidates. If sufficient funds on acceptable terms are not available when needed, we could be required to significantly reduce operating expenses and delay, reduce the scope of, or eliminate one or more of our development programs, which may have a material adverse effect on our business, results of operations and financial condition.

In addition, unforeseen circumstances may arise, or our strategic imperatives could change, causing us to consume capital significantly faster than we currently anticipate, requiring us to seek to raise additional funds sooner than expected. We have no committed external sources of funds.

The amount and timing of our future funding requirements will depend on many factors, including, but not limited to:

the rate of progress and cost of our trials and other product development programs for our product candidates;

the costs and timing of in-licensing additional product candidates or acquiring other complementary companies;

the timing of any regulatory approvals of our product candidates;

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our ability to successfully launch our products and to continue to increase the level of sales in the marketplace;

the actions of our competitors and their success in selling competitive product offerings;

the costs of establishing sales, marketing, manufacturing and distribution capabilities for our products; and

the status, terms and timing of any collaborative, licensing, co-promotion or other arrangements.

Additional financing may not be available when we need it or may not be available on terms that are favorable to us, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. If adequate funds are not available to us on a timely basis, or at all, we may be required to delay, reduce the scope of or eliminate one or more of our development programs or our commercialization efforts.

We have never recognized any revenues from our own sales of our products, and we may never achieve or maintain profitability.

Our ability to become profitable depends upon our ability to generate revenues from sales of our products and our product candidates. To date, we have not recognized any significant revenues from our own sales of our products or product candidates and have incurred significant operating losses. Our historical revenues have been generated through fees for development services and payment for the achievement of specified development, regulatory and sales milestones, as well as royalties, on product sales of Oracea, Sanctura XR and Intuniv licensed products. In May 2009, in exchange for a one-time, lump-sum payment, we licensed all of our rights for Intuniv to an affiliate of Shire plc on a royalty-free, fully paid-up basis. In addition, in connection with our sale of all of our equity interests in Royalty Sub in December 2011, the purchaser acquired all of our license rights to Sanctura XR and Oracea. Accordingly, we no longer generate any revenues from those products.

Our ability to generate product revenues is dependent on our ability to successfully commercialize Oxtellar XR, and, if approved, Trokendi XR. Our ability to successfully commercialize our products depends on, among other things:

generating revenue from the sale of Oxtellar XR;

our obtaining final regulatory approval of Trokendi XR; and

our manufacturing of commercial quantities of our approved products, including Oxtellar XR, at acceptable cost levels.

After our product candidates are approved for commercial sale, we anticipate incurring significant costs associated with commercialization. It is possible that we will never have sufficient product sales revenues to achieve profitability.

Our operating results may fluctuate significantly.

We expect our operating results to be subject to quarterly and annual fluctuations. We expect that any revenues we generate will fluctuate from quarter to quarter and year to year as a result of the timing, market acceptance of our products, and amount of development milestones and royalty revenues received under our collaboration license agreements.

Once we commercialize one or more of our products, our net loss and other operating results will be affected by numerous factors, including:

variations in the level of expenses related to our development programs;

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the success of our bioequivalence and clinical trials through all phases of clinical development;

any delays in regulatory review and approval of product candidates in clinical development;

potential side effects of our future products that could delay or prevent commercialization or cause an approved drug to be taken off the market;

any intellectual property infringement lawsuit in which we may become involved;

our ability to establish an effective sales and marketing infrastructure;

our dependency on third-party manufacturers to supply or manufacture our product candidates;

competition from existing products or new products that may emerge;

regulatory developments affecting our products and product candidates;

our execution of any collaborative, licensing or similar arrangements, and the timing of payments we may make or receive under these arrangements;

the achievement and timing of milestone payments under our existing collaboration and license agreements; and

the level of market acceptance for any approved product candidates and underlying demand for that product and wholesalers' buying patterns.

Due to the various factors mentioned above, and others, the results of any prior quarterly period should not be relied upon as an indication of our future operating performance. If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially.

Prior to May 1, 2012 we operated as a private company and therefore, have limited experience operating as a public company and complying with public company obligations. Complying with these requirements has increased our costs and requires additional management resources, and we still may fail to meet all of these obligations.

We face increased legal, accounting, administrative and other costs and expenses as a public company. Compliance with the Sarbanes-Oxley Act of 2002, the Dodd-Frank Act of 2010, as well as rules of the Securities and Exchange Commission and Nasdaq, for example, has resulted in significant initial cost to us as well as ongoing increases in our legal, audit and financial compliance costs, particularly after we are no longer an "emerging growth company." The Securities Exchange Act of 1934, as amended, or the Exchange Act, requires, among other things, that we file annual, quarterly and current reports with respect to our business and financial condition. Our board of directors, management and other personnel need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations make it more difficult and more expensive for us to obtain director and officer liability insurance, and require us to incur substantial costs to maintain the same or similar coverage.

As a public company, we are subject to Section 404(a) of the Sarbanes-Oxley Act relating to internal controls over financial reporting and we expect to incur significant expense and devote substantial management effort toward ensuring compliance with Section 404(a). We currently do not have an internal audit group, and we will need to hire additional accounting and financial staff with appropriate public company experience

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and technical accounting knowledge. Implementing any appropriate changes to our internal controls may require specific compliance training for our directors, officers and employees, entail substantial costs to modify our existing accounting systems, and take a significant period of time to complete. Such changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce

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accurate consolidated financial statements or other reports on a timely basis, could increase our operating costs and could materially impair our ability to operate our business. We cannot assure you that our internal controls over financial reporting will prove to be effective.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404(a) of the Sarbanes-Oxley Act, or the subsequent testing by our independent registered public accounting firm conducted in connection with Section 404(b) of the Sarbanes-Oxley Act after we no longer qualify as an "emerging growth company," may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our consolidated financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common stock.

We are required to disclose changes made in our internal control procedures on a quarterly basis and our management is required to assess the effectiveness of these controls annually. However, for as long as we are an "emerging growth company" under the recently enacted JOBS Act, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting pursuant to Section 404. We could be an "emerging growth company" for up to five years. An independent assessment of the effectiveness of our internal controls could detect problems that our management's assessment might not. Undetected material weaknesses in our internal controls could lead to financial statement restatements and require us to incur the expense of remediation.

Our ability to use net operating loss and tax credit carryforwards and certain built-in losses to reduce future tax payments is limited by provisions of the Internal Revenue Code, and may be subject to further limitation as a result of the transactions contemplated by the recent follow-on offering in November 2012.

Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, contain rules that limit the ability of a company that undergoes an ownership change, which is generally any change in ownership of more than 50% of its stock over a three-year period, to utilize its net operating loss and tax credit carryforwards and certain built-in losses recognized in years after the ownership change. These rules generally operate by focusing on ownership changes involving stockholders owning directly or indirectly 5% or more of the stock of a company and any change in ownership arising from a new issuance of stock by the company. Generally, if an ownership change occurs, the yearly taxable income limitation on the use of net operating loss and tax credit carryforwards and certain built-in losses is equal to the product of the applicable long term tax exempt rate and the value of the company's stock immediately before the ownership change. We may be unable to offset our taxable income with losses, or our tax liability with credits, before such losses and credits expire and therefore would incur larger federal income tax liability.

In addition, it is possible that the follow-on offering that occurred in November 2012, either on a standalone basis or when combined with future transactions, including issuances of new shares of our common stock, will cause us to undergo one or more additional ownership changes. In that event, we generally would not be able to use our pre-change loss or credit carryovers or certain built-in losses

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prior to such ownership change to offset future taxable income in excess of the annual limitations imposed by Sections 382 and 383 and those attributes already subject to limitations as a result of our prior ownership changes may be subject to more stringent limitations. As of December 31, 2012, we had approximately \$80.8 million of federal net operating loss carryforwards. We also had federal and state research and development tax credit carryforwards of approximately \$4.6 million available to offset future taxable income. These federal and state net operating loss and federal and state tax credit carryforwards will begin to expire at various dates beginning in 2025, if not utilized. In 2011, we completed a study to assess whether an ownership change has occurred, or whether there have been multiple ownership changes since our inception. Due to the significant costs and complexities associated with such study, we have not updated this study in 2012. Accordingly, our ability to utilize the aforementioned carryforwards and tax credits may be limited. As a result, we may not be able to take full advantage of these carryforwards or tax credits for federal and state tax purposes.

Risks Related to Our Indebtedness

Our level of indebtedness and debt service obligations could adversely affect our financial condition, and may make it more difficult for us to fund our operations.

In January 2011, we entered into a secured credit facility pursuant to a loan and security agreement among Oxford Finance Corporation, as collateral agent and lender, and Compass Horizon Funding Company LLC, as lender, which was subsequently amended in December 2011, and promissory notes issued in favor of each lender, providing for term loans of up to an aggregate of \$30.0 million. On January 26, 2011, we drew down our initial \$15.0 million of term loans under our secured credit facility and on December 30, 2011 we drew down the second \$15.0 million. All obligations under our secured credit facility are secured by substantially all of our existing property and assets (excluding our intellectual property) and by a pledge of the capital stock of, subject to certain exceptions, our U.K. subsidiary and any future subsidiary. This debt financing may create additional financial risk for us, particularly if our business or prevailing financial market conditions are not conducive to paying off or refinancing our outstanding debt obligations at maturity. This indebtedness could also have important negative consequences, including:

we will need to repay our debt by making payments of interest and principal, including a final payment of \$750,000 representing 2.5% of the aggregate principal amount of the term loans borrowed under our secured credit facility, which will reduce the amount of money available to finance our operations, our research and development efforts and other general corporate activities;

we may have difficulty obtaining financing in the future for working capital, capital expenditures, acquisitions or other purposes;

our failure to comply with the restrictive covenants in our loan and security agreement could result in an event of default that, if not cured or waived, would accelerate our obligation to repay this indebtedness, and the lenders could seek to enforce their security interests in the assets securing such indebtedness; and

we will be charged a prepayment premium of 2.0% if we prepay the debt within 15 months after the respective amortization dates of the term loans, and a prepayment premium of 1.0% if such prepayment is made thereafter.

To the extent additional debt is added to our current debt levels, the risks described above would increase.

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We may not have cash available to us in an amount sufficient to enable us to make interest or principal payments on our indebtedness when due.

Since our inception in 2005, we have generated no revenue from product sales and have incurred significant operating losses. As of December 31, 2012, we had an accumulated deficit of \$86.3 million. We expect to continue to incur net losses and have negative cash flow from operating activities for the foreseeable future as we continue to develop and seek marketing approval for our product candidates. As a result, we may not have sufficient funds, or may be unable to arrange for additional financing, to pay the amounts due on our outstanding indebtedness under our secured credit facility. Further, funds from external sources may not be available on economically acceptable terms, if at all. For example, if we raise additional funds through collaboration, licensing or other similar arrangements, it may be necessary to relinquish potentially valuable rights to our product candidates or technologies, or to grant licenses on terms that are not favorable to us. If adequate funds are not available when and if needed, our ability to make interest or principal payments on our debt obligations would be significantly limited, and we may be required to delay, significantly curtail or eliminate one or more of our programs.

Failure to satisfy our current and future debt obligations under our secured credit facility could result in an event of default and, as a result, our lenders could accelerate all of the amounts due. In the event of an acceleration of amounts due under our secured credit facility as a result of an event of default, we may not have sufficient funds or may be unable to arrange for additional financing to repay our indebtedness. In addition, our lenders could seek to enforce their security interests in the collateral securing such indebtedness.

We are subject to a number of restrictive covenants which, if breached, could have a material adverse effect on our business and prospects.

Our secured credit facility imposes operating and other restrictions on us. Such restrictions will affect, and in many respects limit or prohibit our ability and the ability of our U.K. subsidiary and any future subsidiary to, among other things