Minerva Neurosciences, Inc.
Form 10-K
March 14, 2016

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2015

OR

¨TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO
Commission File Number 001-36517

Minerva Neurosciences, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware (State or other jurisdiction of incorporation or organization)	26-0784194 (I.R.S. Employer Identification No.)
1601 Trapelo Road, Suite 284 Waltham, MA (Address of principal executive offices)	02451 (Zip Code)

Registrant's telephone number, including area code: (617) 600-7373

Securities registered pursuant to Section 12(b) of the Act: Common Stock, Par Value $0.0001 Per Share; Common Stock traded on the NASDAQ Global Market

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

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES ¨ NO x

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES ¨ NO x

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405) 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, a non-accelerated filer, or a smaller reporting company. See the definition 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 x

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ¨ NO x

The aggregate value of the Company's Common Stock held by non-affiliates of the Company was approximately $86,978,157 as of June 30, 2015, the last day of the Company's most recently completed second fiscal quarter, when the last reported sales price was $5.80 per share.

The number of shares of Registrant's Common Stock outstanding as of March 9, 2016 was 27,760,657.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Definitive Proxy Statement relating to the 2016 Annual Meeting of Stockholders to be filed pursuant to Regulation 14A with the Securities and Exchange Commission are incorporated by reference into Part III

of this Report. Such proxy statement will be filed with the Securities and Exchange Commission not later than 120 days following the end of the Registrant's fiscal year ended December 31, 2015.

MINERVA NEUROSCIENCES, INC.

TABLE OF CONTENTS

All trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners.

This Annual Report on Form 10-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. These forward-looking statements reflect our plans, estimates and beliefs. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “anticipates,” “believes,” “could,” “estimates,” “expects,” “intends,” “may,” “plans,” “potential,” “predicts,” “should,” “would” and similar expressions intended to identify forward-looking statements. Forward-looking statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Because of these risks and uncertainties, the forward-looking events and circumstances discussed in this report may not transpire. These risks and uncertainties include, but are not limited to, the risks included in this Annual Report on Form 10-K under Part I, Item IA, “Risk Factors.”

Given these uncertainties, you should not place undue reliance on these forward-looking statements. Also, forward-looking statements represent our estimates and assumptions only as of the date of this document. You should read this document with the understanding that our actual future results may be materially different from what we expect. Except as required by law, we do not undertake any obligation to publicly update or revise any forward-looking statements contained in this report, whether as a result of new information, future events or otherwise.

Part I

ITEM 1. Business

Overview

We are a clinical-stage biopharmaceutical company focused on the development and commercialization of a portfolio of product candidates to treat patients suffering from central nervous system, or CNS, diseases. Leveraging our scientific insights and clinical experience, we have acquired or in-licensed four development-stage proprietary compounds that we believe have innovative mechanisms of action and therapeutic profiles that can potentially address the unmet needs of patients with these diseases.

Our product portfolio and potential indications include: MIN-101 for the treatment of schizophrenia; MIN-202 (also known as JNJ-42847922), which we are co-developing with Janssen Pharmaceutica NV, or Janssen, for the treatment of insomnia disorder and adjunctive major depressive disorder, or MDD; MIN-117 for the treatment of MDD; and MIN-301 for the treatment of Parkinson’s disease. We believe our product candidates have significant potential to improve the lives of a large number of affected patients and their families who are currently not well-served by available therapies. According to Datamonitor, an independent market research firm, in 2015 approximately 3.2 million people suffered from schizophrenia, 30 million suffered from MDD and 2.0 million suffered from Parkinson’s disease in the United States, Japan and the five major European Union markets of France, Germany, Italy, Spain and the United Kingdom. Insomnia is believed to affect approximately 30 to 35 percent of the global population as estimated by American Academy of Sleep Medicine.

Our management team has extensive experience in the pharmaceutical industry, in particular with respect to CNS products. Dr. Remy Luthringer, our President and Chief Executive Officer, has participated in numerous clinical trials

in the CNS area, including trials for many products approved by the U.S. Food and Drug Administration, or the FDA. Our Executive Vice President, Chief Financial Officer and Chief Business Officer, Geoffrey Race, has worked in the biotechnology industry since 1997 and has served as a chief executive officer or chief financial officer in seven early stage development companies, including Funxional Therapeutics Ltd and PanGenetics BV.

Our Strategy

Our strategy is to develop and commercialize first-in-class products that address critical unmet medical needs in the CNS therapeutic area. We are pursuing this strategy based on the following principles: selection of products with novel mechanisms of action; attention to patient safety and compliance; scientific rigor applied to patient selection and clinical trial conduct; incorporation of patient and caregiver insights to drive clinical advancements; and integrity. Minerva management, as well as the clinical research organizations conducting our trials, have significant experience with study centers and investigators in the countries in which we are conducting our proof-of-principle trials. As a result, we have access to well characterized and validated patient populations and to highly trained physicians with experience in conducting CNS-related trials. With the experience and knowledge base of our clinicians and physicians, we are striving to generate substantive data from these randomized, double blind, placebo-controlled trials that support the clinical advancement of these products in defined patient populations and in multiple regulatory jurisdictions. In summary, key elements of our strategy are:

- Identify, acquire and develop differentiated products based on biological and clinical insights related to the unmet needs of patients;
- Conduct proof-of-principle trials in geographic areas with well characterized and validated patient populations where we have access to highly trained physicians with experience in conducting CNS-related trials;
- Leverage the randomized, double-blind, placebo-controlled data from these trials to advance the clinical development of our product candidates in multiple regulatory jurisdictions;
- Selectively explore collaborations with leading pharmaceutical companies to maximize the value of our current product candidate portfolio, particularly in connection with the initiation of pivotal Phase III clinical trials and subsequent regulatory review, approval and commercialization;
- Apply our management team’s expertise and current intellectual property portfolio to identify and explore additional indications relating to our current portfolio of compounds and to acquire additional product candidates.

Our History

In November 2013, Cyrenaic Pharmaceuticals, Inc., or Cyrenaic, and Sonkei Pharmaceuticals, Inc., or Sonkei, merged, and the combined company was renamed Minerva Neurosciences, Inc. Cyrenaic had been incorporated in 2007 and had exclusively licensed MIN-101 from Mitsubishi Tanabe Pharma Corporation, or MTPC. Sonkei had been incorporated in 2008 and had exclusively licensed MIN-117 from MTPC. We executed the merger as we saw an opportunity to better serve an underserved patient population through combining a portfolio of promising product candidates targeting CNS diseases. As a result of the merger, we have the rights to develop and commercialize MIN-101 and MIN-117 globally, excluding most of Asia.

We further expanded our product candidate portfolio in February 2014 by acquiring the shares of Mind-NRG SA, or Mind-NRG, which had exclusive rights to develop and commercialize MIN-301. In addition, in February 2014 we entered into a co-development and license agreement with Janssen, one of the Janssen Pharmaceutical Companies of Johnson & Johnson. Pursuant to this agreement we are co-developing MIN-202 and have the right to commercialize this compound in the European Union, Switzerland, Liechtenstein, Iceland and Norway, or the Minerva Territory, subject to royalty payments to Janssen, with Janssen having commercialization rights outside of the Minerva Territory, subject to royalty payments to us. Effective January 28, 2016 Mind-NRG converted under Swiss law from an S.A. (public limited liability company) to an S.A.R.L. (company with limited liability).

Our Pipeline

MIN-101

Introduction

MIN-101 is a compound that has been shown to block serotonin receptors and sigma receptors, two receptors in the brain that are involved in the regulation of mood, cognition, sleep and anxiety. We are developing MIN-101 to treat patients with schizophrenia. MIN-101 is meant to block a specific subtype of serotonin receptor called 5-HT2A. When 5-HT2A is blocked, certain symptoms of schizophrenia, such as hallucinations, delusions, agitation and thought and movement disorders, as well as the side effects associated with antipsychotic treatments, can be minimized. Additionally, blocking 5-HT2A promotes slow wave sleep, a sleep stage often disrupted in patients with schizophrenia. MIN-101 is also meant to block a specific subtype of sigma receptor called sigma2, which is involved in movement control, psychotic symptom control and learning and memory. Blocking sigma2 also modulates other neurotransmitters in the brain, in particular dopamine, which is important as individuals with schizophrenia often have elevated levels of dopamine in their brains. Blocking sigma2 also increases calcium levels in neurons in the brain, which can improve memory. Recent literature has also indicated that a sub-type of progesterone protein complex might also be a putative binding site for sigma2 receptors and might explain the effects on cognition of MIN-101.

We believe the scientifically supported and innovative mechanisms of action of MIN-101 may potentially address the unmet needs of this patient population. We plan to initially seek approval of MIN-101 as a first line monotherapy, and we also plan to study its use as an adjunctive therapy. We believe that MIN-101, if approved, could treat the majority of patients diagnosed with schizophrenia. We have recently completed the development of a once-a-day tablet delivery of MIN-101, which is more convenient for patients than the twice-a-day formulation, which was used in previous trials.

We have exclusively licensed MIN-101 and a number of back-up compounds from MTPC. MTPC has retained commercialization rights to MIN-101 in most of Asia.

Clinical Development

Phase IIb Trial

We completed enrollment of a total of 244 patients in a Phase IIb clinical trial of MIN-101 in Europe in December 2015. The trial is being conducted in stable subjects with schizophrenia suffering from predominantly negative symptoms. We are evaluating two doses of MIN-101 (32mg daily and 64mg daily) versus placebo, in a double-blind design in 244 subjects over a core 12-week treatment period. The primary efficacy endpoint in this trial is to evaluate the changes from baseline of negative symptoms after three months of drug administration, as measured from the baseline in the Positive and Negative Symptom Scale, or PANSS.

We are also investigating the effects of MIN-101 on positive symptoms and overall symptoms of schizophrenia measured by PANSS and the Clinical Global Impression rating scales, as well as its effects on sleep, cognition, anxiety and mood, and clinical and biological safety, pharmacokinetics and drug plasma levels. Cognitive function, sleep, and improvement in function are also being evaluated. The dose formulation employed in this trial is the once-daily dose tested in the Phase I single-center, open-label trial described below. We anticipate top line results from the core 12-week treatment evaluation period of the Phase IIb study in the second quarter of 2016.

Patients improving their symptomatology during the first 12 weeks of this study are being provided the opportunity to enter into an extension phase of six months, which will provide additional long term safety and efficacy data. While we are initially pursuing a first line monotherapy indication for MIN-101, we also plan to study MIN-101 as an adjunctive therapy. During contemplated advanced-stage trials for MIN-101, we may also explore co-administration with atypical antipsychotics. We plan to conduct additional DDI (drug-drug interaction) studies, CMC (chemistry, manufacturing and controls) scale up work and carcinogenicity studies.

We have implemented an independent Scientific Advisory Board (SAB) to monitor safety and efficacy data generated in ongoing and future clinical trials with MIN-101, as well as historical data from completed trials with this compound. The SAB's evaluation of MIN-101 data is intended to identify any clinically relevant trends observed in these trials and to provide us with recommendations based on their observations of data. Members of the SAB were appointed based on their respective recognized expertise in the fields of psychiatry, cardiology and biostatistics. Our appointment of the SAB is based on our recognition that increased monitoring of clinical data should accompany long-term patient exposure to the drug, beginning with those patients participating in the six-month extension stage of the Phase IIb trial. The SAB may request unblinded data and make recommendations regarding clinical trial conduct, which we will consider in our decisions regarding any modifications in clinical trials.

We believe there may be an opportunity in future trials to explore the use of MIN-101 in neuropsychiatric diseases outside of schizophrenia, such as severe mood or neurodegenerative disorders. Our Investigational New Drug (IND) application for MIN-101 has become effective, which enables us to initiate clinical trials with this compound in the U.S. We plan to meet with the FDA and the European Medicines Agency (EMA) regarding late-stage clinical development of MIN-101 that builds upon the results of our Phase II trials. Input from the FDA and EMA will be essential in determining the scope and design of any advanced clinical stage program. Such a program may include both independently conducted and partnered trials, as well as accelerated or breakthrough routes to registration depending on the nature of the data from our ongoing Phase II trials. We plan to communicate details about our next

steps in the development of MIN-101 after data from the Phase II trials become available and after subsequent discussions with regulatory authorities.

Phase IIa Trial

In 2009 we completed a Phase IIa trial of MIN-101 in subjects suffering from schizophrenia. Enrolled subjects had previously suffered from an acute episode requiring hospitalization. This was a double-blind, placebo controlled study with a three month treatment period in which 96 subjects were randomized and 30 completed the study protocol. Patients suffered from positive, negative and cognitive symptoms and had ceased to respond well to previously prescribed medication. Subjects received either placebo or MIN-101, including doses and at a dosing schedule that may differ from the final formulated dose.

The primary endpoint of the study was the efficacy of MIN-101 versus placebo, as measured by PANSS total and sub-scores after one month of treatment. The PANSS is used to measure psychopathology in patients suffering from schizophrenia and can be split into either three factors (positive, negative and general psychopathology) or in five factors (positive, negative, activation, dysphoric mood and autistic thoughts). Secondary and exploratory endpoints included the efficacy of MIN-101 versus placebo through the PANSS total and sub scores after three months of treatment, as well as cognition, mood, anxiety and sleep using various psychological scales at various treatment time points.

In the Phase IIa trial, subjects treated with MIN-101 showed ongoing improvements in negative symptoms, as compared to baseline, throughout the duration of the trial. After one month, improvements on the PANSS negative symptoms scale were observed. Because this Phase IIa trial was not powered to show results with statistical significance, the study’s primary endpoint was not met. After three months of treatment, the MIN-101 group showed improvements in negative symptoms as compared to placebo.

Subjects participating in this clinical trial receiving MIN-101 or placebo experienced adverse events, including, but not limited to gastrointestinal, nervous system, psychiatric, and cardiac events, with two subjects with increased heart rate and one subject with decreased heart rate that were deemed to be possibly related to MIN-101 by investigators. Generally, with the exception of cardiac events, which occurred in the MIN-101 subjects alone, similar adverse events were seen in the placebo group tested in this study, although at different rates. The safety results of the Phase IIa study supported Phase I results observed in healthy volunteers, and we will assess additional safety data generated in future clinical trials that explore the intended therapeutic dose and dosing schedule, including the ongoing Phase IIb trial.

MIN-117

Introduction

MIN-117 is a compound we are developing to treat patients suffering from MDD, the most prominent subtype of depression. Patients suffering from MDD experience feelings of sadness, loss, anger or frustration that interfere with their ability to carry out and enjoy once-pleasurable activities. While suicide is the leading cause of death in those with MDD, other factors, such as changes in immune function and susceptibility to disease, can also lead to early mortality.

We believe MIN-117 has the potential to address limitations of existing therapies, such as slow onset of action and poor safety and tolerability, without many of the typical side effects associated with currently approved therapies. The pharmacological effects of MIN-117 are related to serotonin and dopamine, two neurotransmitters in the brain. MIN-117 is meant to block a specific subtype of serotonin receptor called 5-HT1A. When 5-HT1A is blocked, anxiety and mood can be regulated. In addition, MIN-117 is meant to prevent the reuptake of serotonin and dopamine, which increases the amount of serotonin and dopamine in the brain, which is tied to an improvement in mood in individuals suffering from MDD. MIN-117 is also meant to modulate the levels of Alpha-1a and 1b, which further modulates serotonin and dopamine.

Based upon clinical and pre-clinical studies completed to date, we believe MIN-117 will demonstrate a safety profile comparable to placebo without many of the typical side effects of current MDD treatments, including cognitive impairment, sexual dysfunction, sleep disorders and weight gain. As part of our license agreement with MTPC, we may develop, sell, and import products related to the MIN-117 compound globally, excluding most of Asia. In the second quarter of 2015, we initiated a Phase IIa clinical trial in Europe. Enrollment in this trial is now complete, and we expect top line results to be available in the second quarter of 2016.

Clinical Development

Phase IIa Trial

In the first quarter of 2016, we completed enrollment of 84 patients with MDD in a Phase IIa, randomized, double-blind, parallel group, placebo and active controlled clinical trial with MIN-117 in Europe, comparing MIN-117 to Paroxetine and placebo over six weeks of treatment. The primary endpoint of this study is to evaluate the efficacy of MIN-117 given at 0.5 mg and 2.5 mg daily in reducing the symptoms of a major depressive episode as measured by the change from baseline in the Montgomery-Asberg Depression Rating Scale, or MADRS, total score over six weeks of treatment. Patients with a minimum score of depression of 30 points assessed via MADRS were enrolled. The control molecule is 20mg of Paroxetine, a dose shown in previous trials to improve depressive symptoms in MDD patients suffering from a major depressive episode.

The main secondary endpoints are the efficacy of MIN-117 versus placebo in onset of antidepressant response as measured by the change from Baseline in MADRS total score over 2 weeks of treatment. In addition, we will evaluate global change from baseline versus placebo in severity of illness and improvement using the Clinical Global Impression of Severity Scale and Clinical Global Impression of Improvement Scale, or CGI S and CGI-I, over 6 weeks of treatment. Additional secondary endpoints include the evaluation of MIN-117 versus placebo and paroxetine on sexual functioning, cognition and objective and subjective sleep measures. Safety, tolerability and plasma levels will also be evaluated.

We expect to announce top line data from the Phase IIa trial with MIN-117 in the second quarter of 2016. The efficacy and safety data from the Phase IIa trial will guide our discussions with regulatory authorities regarding the nature of potential future clinical development of this compound. We plan to communicate details about our the next steps in the development of MIN-117 after Phase IIa data become available and pending future discussions with regulatory authorities.

MIN-202

Introduction

MIN-202 is an innovative selective orexin 2 receptor antagonist we are co-developing with Janssen for the treatment of insomnia. Insomnia is the repeated difficulty with sleep initiation, maintenance or quality that occurs despite adequate time and opportunity for sleep, resulting in daytime impairment. Insomnia can be the primary condition for patients or a secondary symptom of, and contributor to, another medical or psychiatric condition, such as MDD or schizophrenia. We intend to evaluate MIN-202 as a treatment in primary insomnia, as well as in comorbid insomnia as an adjunctive therapy with an antidepressant for the treatment of mood disorders. According to the American Academy of Sleep Medicine, approximately 30 percent of adults have symptoms of insomnia. Additionally, the National Sleep Foundation estimates that nearly 70 percent of individuals with insomnia experience symptoms for one year, and half still have insomnia for as long as three years.

In the brain, the orexin system is involved in the control of several key functions, including metabolism and wakefulness. MIN-202 seeks to inhibit the activity of the neurons that promote wakefulness by selectively blocking the orexin 2 receptor. Rather than making an individual sleepier, blocking the orexin 2 receptor reduces the level of the neurotransmitters that signal the brain to maintain vigilance and wakefulness, which can be helpful for patients with insomnia.

We are co-developing MIN-202 with Janssen and own the exclusive rights to develop and commercialize the compound in the Minerva Territory subject to royalty payments to Janssen and have the right to receive royalties on any sales outside the Minerva Territory. Janssen completed a Phase I single ascending dose study of MIN-202 in 2011 that suggested a relationship which supports a rapid induction and promotion of sleepiness.

Clinical Development

Phase IIa Trial

In January 2016 we announced top line results from a Phase IIa trial with MIN-202 in insomnia disorder. Patients treated with MIN-202 in this trial were observed to have statistically significant improvements in key sleep parameters, compared to patients treated with placebo. These parameters include sleep efficiency (SE) as measured by objective polysomnography, the primary endpoint of the trial, for which a positive efficacy signal was detected for 40 milligrams MIN-202 versus placebo ($p<0.001$). Additional significant positive efficacy signals were observed for key secondary parameters in this trial, including latency to persistent sleep (LPS), wake after sleep onset (WASO), and total sleep time (TST). Compared to placebo, MIN-202 was observed to significantly improve polysomnography parameters ($p<0.001$) on Days 1 and 5. On Day 5, LPS and WASO were reduced by 23.2 and 11 minutes and TST and SE increased by 39 minutes and 8.12 percent, respectively. Subjectively estimated TST, LPS, and WASO also improved versus PLA by 43.1, -38.8, and -14.8 minutes, respectively. No serious adverse events were observed in this trial, and preliminary data indicate that MIN-202 was well tolerated by patients. The most common treatment-emergent adverse events associated with exposure to MIN-202 during the double-blind phase of the study were somnolence and abnormal dreams.

The Phase IIa trial was a randomized, two way, cross-over, placebo-controlled double-blind study to evaluate the effect of MIN-202 on sleep and daytime functioning in 28 patients with insomnia disorder without psychiatric co-morbidity. Patients were given MIN-202 or placebo in a cross-over design for treatment periods of five days, separated by a washout period. The trial was conducted at clinical sites in the U.S. and Europe. Complete results,

including subjective evaluations and their correlation with objective PSG measures, are planned for peer-reviewed presentation in the future.

Phase I Trials

On March 11, 2016, we announced favorable top line results from the Phase Ib clinical trial in MDD with MIN-202. MIN-202 was observed to be well tolerated by study participants over a one-month treatment duration, with no serious adverse events. Consistently greater improvements in depressive symptomatology were observed in patients randomized to receive MIN-202 compared to those randomized to receive placebo (PLA) or diphenhydramine (DPH), as measured by clinician administered rating scales, including the Hamilton Depression Rating Scale ($HDRS_{17}$). Core symptoms of depression (as measured by the $HAM\text{-}D_6$) were observed to be significantly improved in the MIN-202 arm when compared with PLA.

The Phase 1b trial was a randomized, multi-center, double-blind, parallel group, diphenhydramine- and placebo-controlled study to evaluate the effect of MIN-202 in MDD outpatients 18-65 years of age. Forty-eight participants were enrolled in three groups that received doses of 20 milligrams (mg) of MIN-202 daily, 25 mg of diphenhydramine daily (used as a positive control to induce sedation, due to its H1 anti-histaminergic activity, with no/limited expected antidepressant efficacy at the selected dose level) or placebo over four weeks. Patients were either anti-depressant naïve or treated with a maximum of two concurrent antidepressants. The primary endpoint was safety and tolerability, and secondary endpoints included assessments of depressive symptomatology, cognition and sleep. The trial was conducted at seven clinical sites in Europe.

In February 2016, we announced top line data from a Phase I clinical trial with MIN-202 conducted in Japan. It was observed that single dose morning administration of MIN-202 was well tolerated at all three dose levels tested, 5 milligrams (mg), 20 mg and 40 mg. The observed plasma pharmacokinetic features were comparable to those observed in previous trials carried out in healthy non-Asian study participants. No clinically relevant safety concerns were observed based on the assessment of multiple safety endpoints. Somnolence was the most frequently reported adverse event at the two higher doses, an expected finding as this compound is being developed as a treatment for patients suffering from insomnia disorder and as adjunctive treatment to concomitant antidepressant drug therapy in MDD. This trial was a single center, double blind, placebo-controlled randomized single ascending dose study to investigate the safety, tolerability and pharmacokinetics of MIN-202 in 24 healthy Japanese adult male study participants.

MIN-301

We are developing MIN-301, a soluble recombinant form of the Neuregulin-1b1, or NRG-1b1, protein, for the treatment of Parkinson's disease. We believe MIN-301 has the potential to slow the onset of, and restore the brain tissue damage caused by, the disease. MIN-301 is produced by recombinant technology, which is a type of process that modifies the genetics of a biological organism to cause it to produce a particular product. MIN-301 uses an Escherichia coli organism to produce neuregulin-1b1, a peptide. Once administrated, this peptide binds to a particular receptor, ErbB4, which produces certain biological effects. For instance, binding to ErbB4 modulates the levels of certain neurotransmitters such as GABA and glutamate in the brain, which are often unbalanced in individuals with Parkinson's disease. Further, ErbB4 promotes oxygenation and metabolism of neurons, which could indicate MIN-301 could reverse the damage caused by Parkinson's disease.

Parkinson's disease is a progressive and incurable disease that leads to disability and lower quality of life. According to Datamonitor, there were more than 700,000 cases in the United States, Japan and the five key European markets in 2015, and Parkinson's disease was identified as the 14th leading cause of death by the Centers for Disease Control and Prevention in 2013. Current treatments for Parkinson's disease improve the symptoms of patients, but none have been proven to delay the onset of the disease, slow or prevent the progression of the disease or reverse its effects. Due to MIN-301's novel mechanism of action that targets neurological deficits, we believe MIN-301 has the potential to address these unmet needs of patients and, if approved, may be used as an early-stage monotherapy as well as a complementary therapy to existing treatments.

In January 2015 we announced results from a non-human primate study showing that treatment with an analog of MIN-301 resulted in improvements in a range of symptoms associated with a Parkinson's disease model in primates. The results confirmed the beneficial effects of MIN-301 in non-primate preclinical models.

The mechanism of action of MIN-301 is still under further investigation, but we believe our protein has important characteristics, such as effects on oxidative stress reversal, effects on cell metabolism particularly adenosine triphosphate, or ATP, and effects on GABA and glutamate. Taken together, we believe the effects described above could protect dopaminergic neurons, which is a key element in the cause of Parkinson's disease, and possibly on other sub-types of neurons and other brain cells such as glial cells. This indicates that MIN-301 may have a novel neuro-protecting and neuro-restorative profile. In view of this MIN-301 mechanism of action and based on a number of other studies performed by other research labs on neuregulin, we believe several other indications of the molecule

may be pursued, such as for Alzheimer's disease and other neuro-degenerative disorders, such as multiple sclerosis, and for other psychological disorders, such as schizophrenia, stroke and traumatic brain injury.

Our next steps for the development for MIN-301 include continuing to conduct preclinical studies in preparation for an Investigational New Drug, or IND, or Investigational Medicinal Product Dossier, or IMPD filing, with a Phase I study expected to commence thereafter.

License Agreements

MIN-101 License Agreement with MTPC

We have entered into a license agreement with MTPC dated as of August 30, 2007, as amended, or the MIN-101 License Agreement. Under the terms of the MIN-101 License Agreement, we acquired an exclusive license to the lead compound known as CYR-101 (subsequently renamed MIN-101), and other compounds with a similar structure and intended purpose and other data included within the valid claims of certain patents licensed to us under the MIN-101 License Agreement. The license is for world-wide rights other than certain countries in Asia, including China, Japan, India and South Korea. We will pay MTPC a tiered royalty for net sales of product by us or any of our affiliates or sublicensees containing the licensed compound at a range of percentages of the high single digits to the low teens depending on net sales of products under the MIN-101 License Agreement. We were also required to make certain milestone payments upon the achievement of certain development and commercial milestones, potentially up to $57.5 million for MIN-101 and up to $59.5 million for additional products.

In January 2014, we renegotiated the structure of the license for MIN-101 such that we are required to make milestone payments upon the achievement of one development milestone totaling $0.5 million and certain commercial milestones, which could total up to $47.5 million, in the aggregate. In addition, in the event that we sell the rights to the license, MTPC will be entitled to a percentage of milestone payments in the low teens and a percentage of royalties received by us in the low double digits. This license agreement has a term of the later of 12 years from the launch of the product in each country in our territory, or the expiration of our obligation to pay royalties, upon which we will have a fully paid-up, non-exclusive, perpetual, irrevocable license. Our obligation to pay royalties continues, on a country-by-country basis, until the expiration of the last-to-expire patent that covers MIN-101 in each country in our territory.

MIN-117 License Agreement with MTPC

Sonkei entered into a license agreement with MTPC dated September 1, 2008, as amended, or the MIN-117 License Agreement. Under the terms of the MIN-117 License Agreement, we acquired an exclusive license to the lead compound known as SON-117 (subsequently renamed MIN-117) and other data included within the valid claims of certain patents licensed to us under the MIN-117 License Agreement. Sonkei paid MTPC an initial license fee of $0.5 million. The license is for world-wide rights other than certain countries in Asia, including China, Japan, India and South Korea. We will pay a tiered royalty for net sales of product by it or any of its affiliates or sublicensees containing the licensed compound ranging from the high single digits to the low teens depending on net sales of products under the MIN-117 License Agreement. Through the date of the agreement, as amended, we were required to make payments up to $57.5 million upon the achievement of certain commercial milestones.

In January 2014, we renegotiated the structure of the license for MIN-117 such that we are required to make certain milestone payments upon the achievement of certain commercial milestones up to $47.5 million. In addition, in the event that we sell the rights to the license, MTPC will be entitled to a percentage of milestone payments in the low teens and a percentage of royalties received by us in the low double digits. This license agreement has a term of the later of 10 years from the launch of the product in each country in our territory, or the expiration of our obligation to pay royalties, upon which we will have a fully paid-up, non-exclusive, perpetual, irrevocable license. Our obligation to pay royalties continues, on a country-by-country basis, until the expiration of the last-to-expire patent that covers MIN-117 in each country in our territory. In April 2015, the Company amended the diligence milestone obligation under the license agreement for MIN-117 to extend the deadline from April 30, 2015 to June 30, 2015 to begin enrollment in a Phase IIa or Phase IIb study with MIN-117 in patients suffering major mood disorders. As consideration for the two-month extension, the Company paid MTPC, and recorded an expense for, $80,000 in May 2015. The Company met the enrollment milestone obligation in June 2015.

MIN-202 Co-Development and License Agreement with Janssen

We have entered into a co-development and license agreement with Janssen, dated as of February 12, 2014, pursuant to which, among other things, Janssen has granted us an exclusive license (even as to Janssen), with the right to sublicense, in the European Union, Switzerland, Liechtenstein, Iceland and Norway, referred to as the Minerva Territory, under certain Janssen patent and patent applications to sell products containing any orexin 2 compound, controlled by Janssen and claimed in a Janssen patent right, as an active ingredient, or MIN-202, for any use in humans. In addition, upon regulatory approval in the Minerva Territory (and earlier if certain default events occur), we will have rights to manufacture or have a third party manufacture MIN-202. We have granted to Janssen an exclusive license, with the right to sublicense, under all patent rights and know-how controlled by us related to any orexin 2 compound, controlled by Janssen and claimed in a Janssen patent right, as an active ingredient, or MIN-202, to sell MIN-202 outside the Minerva Territory. This agreement will be in place until we have no further payment obligations, upon which we will have a non-exclusive, fully paid-up and royalty-free license in the Minerva Territory. We will also have the right of first negotiation for any sublicense that Janssen pursues in certain Asian and Latin American

countries and the United States. Our obligation to pay royalties begins upon the first commercial sale of a licensed product in each country in which we have licensing rights and continues until the later of 10 years, the expiration of the last to expire intellectual property right owned by Janssen or the end of the period during which the licensed product is subject to regulatory exclusivity in each country.

In consideration of the licenses granted, we made an initial upfront payment of $22.0 million and will pay a quarterly royalty in the high single digits (subject to certain customary adjustments) on the aggregate net sales for MIN-202 products sold by us, our affiliates and sublicensees in the European Union. Janssen will pay a quarterly royalty in the high single digits (subject to certain customary adjustments) on the aggregate net sales for MIN-202 products sold by Janssen outside the European Union.

We will pay 40% of MIN-202 development costs related to the joint development of any MIN-202 products. However, subject to certain exceptions, our share of aggregate development costs may not exceed (i) $5.0 million for the period beginning from the effective date of the Janssen license and ending following the completion of certain Phase Ib clinical trials and animal toxicology studies and (ii) $24.0 million for the period beginning from the effective date of the Janssen license and ending following the completion of certain Phase II clinical trials.

Janssen has a right to opt out at the end of certain development milestones, with the first milestone being the completion of a single day Phase I clinical trial in patients with MDD. Upon opt out, Janssen will not have to fund further development of MIN-202 and the Minerva Territory will be expanded to also include all of North America. We would then owe Janssen a reduced royalty in the mid-single digits for all sales in the Minerva Territory.

We have the right to terminate the Janssen license following certain development milestones, the first of which is the completion of a certain Phase Ib clinical trial in patients with insomnia and certain toxicology studies in animals. If we terminate the Janssen license within 45 days of this milestone, we must pay Janssen a termination fee equal to $3.0 million. If we terminate the Janssen license at any time following the last development milestone involving a certain Phase IIb clinical trial, we will be entitled to a royalty in the mid-single digits from sales of MIN-202 by Janssen.

Janssen may also terminate the agreement for our material breach or certain insolvency events, including if we are unable to fund our portion of the development costs.

Competition

MIN-101: Competition in the Pharmaceutical Market for the Treatment of Schizophrenia

Current drug therapies for the treatment of schizophrenia mainly target the positive symptoms of the disease. When patients present positive symptoms and require treatment, they are typically given either conventional “first-generation” antipsychotic medication, such as GlaxoSmithKline’s Thorazine Sanofi-Aventis’ Largactil (chlorpromazine) and Johnson & Johnson’s Haldol (haloperidol), or second-generation “atypical antipsychotics,” such as Novartis’ Clozaril (clozapine), Johnson & Johnson’s Risperdal (risperidone), AstraZeneca’s Seroquel (quetiapine), Eli Lilly’s Zyprexa (olanzapine) and Bristol-Myers Squibb’s Abilify (aripiprazole).

Both types of existing therapies have limited ability to improve negative symptoms, cognitive symptoms and insomnia. In addition, existing therapies have extensive side effects such as weight gain, metabolic syndrome, sedation, nausea, movement disorders, restlessness, insomnia, impairment of cognitive skills, and prolactin increase. Since schizophrenia has a wide range of symptoms, multiple therapeutics are often prescribed in an attempt to address all aspects of the disease, compounding these side effects.

Given the focus of current drug therapies on positive symptoms and their side effect profiles, we believe current drug therapies are unlikely to be directly competitive with MIN-101, which is intended to target the spectrum of schizophrenia symptoms. However, new drug therapies in addition to MIN-101 are being developed to address the limitations of current therapies. Two new pharmacological approaches have been investigated. One targets a neurotransmitter called glutamate and the other targets a neurotransmitter called nicotine. Glutamate is the most predominant neurotransmitter system in maintaining the brain in an active state and is involved in maintaining accurate vigilance, attention and contributing to some cognitive skills. Nicotine is among the most predominant neurotransmitter system involved in learning and some other cognitive skills. Even though there are several compounds still under development, recent clinical data of the most advanced molecules following these two mechanisms of action have shown limited effectiveness.

MIN-117: Competition in the Pharmaceutical Market for the Treatment of MDD

The pharmaceutical market for the treatment of MDD is largely comprised of selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs) and atypical antipsychotics. By the time of MIN-117’s estimated launch, if approved by the FDA, a number of these high-selling antidepressants will be generic, and would be key competitors to MIN-117. These products include Forest’s Lexapro/Cipralex (escitalopram), Pfizer’s Zoloft (sertraline), GlaxoSmithKline’s Paxil/Seroxat (paroxetine), Eli Lilly’s Prozac (fluoxetine), Forest’s Viibryd

(vilazodone), Pfizer's Effexor (venlafaxine), Pfizer's Pristiq (desvenlafaxine), Eli Lilly's Cymbalta (duloxetine), AstraZeneca's Seroquel (quetiapine) and Bristol-Myers Squibb's Abilify (aripiprazole).

Both SSRIs and SNRIs have significant limitations. SSRIs may lead to varying levels of weight gain and the impairment of cognitive skills and sexual function. In some cases, SNRIs have a worse safety and tolerability profile compared to SSRIs, in particular with respect to cardiovascular side effects. In addition, SSRIs and SNRIs are effective in only a part of the MDD patient population. Over one-third of patients fail to respond to two or more successive lines of antidepressant therapy.

Patients with TRMD often require treatment with several antidepressants, such as an SSRI or SNRI, combined with an "adjunct" therapy such as an antipsychotic or mood stabilizer. These antipsychotic compounds, such as AstraZeneca's Seroquel (quetiapine) and Bristol-Myers Squibb's Abilify (aripiprazole), and mood stabilizers, such as Janssen Pharmaceuticals' Topamax (topiramate), cause some slight improvements in efficacy but often have unacceptable side effects, including motor symptoms, sedation, lack of concentration, and weight gain.

MIN-117 may have a faster onset of action, fewer side effects than existing treatments, and could benefit non- or partial-responders, but a number of products in development could also compete with MIN-117. Lundbeck's Vortioxetine (Brintellix), an SSRI with additional 5-HT receptor modulation activity, has been developed as a monotherapy and was recently approved by the FDA for use as a second-line therapy. Brintellix has been shown to have fewer side effects, in particular less impact on cognition, than existing therapies, though it does not show improved efficacy on depressive symptoms. In addition, Eli Lilly's edivoxetine, a norepinephrine reuptake inhibitor, and Naurex's GL4X-13 and AstraZeneca's AZD6765, both targeting the NMDA receptor, are expected to have a faster onset of therapeutic effect as compared to currently available therapies.

MIN-202: Competition in the Pharmaceutical Market for the Treatment of Insomnia

Most of the pharmaceuticals on the market for insomnia target neurotransmitter pathways involved in depressing the brain activity, such as the histamine and GABA pathways, to induce a decrease in vigilance and attention, leading to sedation and sleep induction. The leading molecule among the current third generation of GABAergic drugs is Sanofi's zolpidem, often marketed under the name Ambien, and is available in generic form. However, zolpidem requires careful utilization to avoid tolerance and drug abuse and extensive sleep studies have demonstrated that zolpidem does not restore physiological sleep and does not allow restorative sleep, which prevents good daytime performance.

Unlike existing therapies, MIN-202, if approved, is expected to inhibit wakefulness-promoting neurotransmitters, rather than activating sleep-promoting neurotransmitters. In August 2014, Merck & Co.'s dual orexin receptor antagonist, suvorexant, was approved by the FDA and is currently marketed under the name Belsomra®. We believe that Belsomra may be the only new insomnia pharmaceutical product to launch significantly in advance of MIN-202's launch. If approved, we believe MIN-202, which is a single orexin receptor antagonist that targets orexin 2 pathways only and has a different pharmacokinetic profile from Belsomra, will have equal or superior efficacy, less residual sedation and impaired daytime functioning, and superior preservation of appropriate levels of REM as compared to Belsomra.

MIN-301: Competition in the Pharmaceutical Market for the Treatment of Parkinson's Disease

Current treatments for Parkinson's disease are intended to improve the symptoms of patients. The cornerstone of Parkinson's therapy is levodopa, as it is the most effective therapy for reducing symptoms of Parkinson's disease. However, levodopa may cause unpleasant systemic side effects, such as dyskinesias, and is often used with dopaminergics, such as DDIs, to manage these side effects. While initially effective, symptoms become increasingly difficult to control over time, and patients experience a pattern of motor complications that include motor fluctuations, dyskinesias, off-period dystonia, freezing and falls. Accordingly, there are advantages to deferring their use to later stages of the disease, or using them with other therapies to reduce the side effects of motor fluctuations and dyskinesia that 50% of levodopa patients experience.

Unlike currently available therapies, MIN-301, if approved, is intended to delay the onset of the disease, slow or prevent the progression of the disease or reverse its effects. Since MIN-301 is expected to target Parkinson's disease, rather than merely its symptoms, and current therapies are not fully effective at improving the symptoms of Parkinson's disease without side effects, we believe that levodopa and other currently available generic products may not be directly competitive with MIN-301. While there are other drug therapies in development that will target the disease, such as gene and stem cell therapy and A2A receptor agonists, the majority of products in development for Parkinson's disease are still in the pre-clinical stage.

Intellectual Property

We strive to protect the proprietary products and technologies that we believe are important to our business, including seeking and maintaining patent protection intended to cover the composition of our product candidates, their methods of use, related technology and other inventions that are important to our business, to the extent such protection is available. As more fully described below, patent applications have been filed by us or our licensors covering compositions of matter for and methods of using our product candidates MIN-101, MIN-117, MIN-202 and MIN-301, and other inventions. We also rely on trade secrets and careful monitoring of our proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

The patent portfolios for our product candidates are summarized below.

MIN-101 (Formerly Developed by Cyrenaic Pharmaceuticals)

Our Owned Patent Applications Directed to MIN-101

We own several patent applications that claim methods of use of MIN-101 to treat schizophrenia, treat or diminish symptoms of schizophrenia, treat disorders or parameters of sleep, treat sigma-2 mediated disorders or conditions, and treat symptoms of sigma-2 mediated disorders or conditions. Applications are pending in the United States and Brazil, Canada, China, Europe, Hong Kong, Indonesia, Japan, Korea, Russia and Taiwan. We have received a notice of intent to grant in both the Russian and Taiwanese applications

If granted, the patent terms of these applications expire no earlier than July 20, 2031.

We also filed applications directed to formulations and polymorphs of MIN-101. Applications are pending in the United States, Taiwan and the PCT.

If granted, the patent terms of these applications expire no earlier than November 30, 2035.

MIN-101 Patents and Applications Licensed to Us

Our MIN-101 patent portfolio further consists of exclusive licensed patent rights, including U.S. Patent No. 7,166,617 directed to MIN-101 compositions of matter. We also license patents directed to MIN-101 composition and methods of treating central nervous system diseases in Europe, Australia, Canada, Israel, New Zealand, and Russia. The EP ‘512 patent is validated in the following EU states: Austria, Belgium, The Republic of Cyprus, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Latvia, Lithuania, Luxembourg, Macedonia, Monaco, The Netherlands, Portugal, Romania, Slovenia, Spain, Sweden, Switzerland, Turkey, and The United Kingdom.

The foreign patents expire no earlier than February 26, 2021. The US ‘617 patent expires no earlier than May 17, 2021. Patent term extensions of up to five years may be available in the United States.

As part of the license agreement, Minerva may also make, sell, and import products related to the MIN-101 compound in the rest of the world except in MTPC territories. which include the Asia-Pacific region and specifically consists of the countries of Bangladesh, Brunei, India, Indonesia, Japan, Malaysia, Pakistan, the People’s Republic of China (including Hong Kong), the Philippines, Singapore, South Korea, Sri Lanka, Taiwan, Thailand, and Vietnam.

Ongoing development and clinical trials may lead to additional patent applications directed to MIN-101.

MIN-117 (Formerly Developed by Sonkei Pharmaceuticals)

Our Owned Patent Applications Directed to MIN-117

We own patent applications filed in the United States Australia, Brazil, , Canada, Chile, China, Colombia, Europe, India, Indonesia, Israel, Japan, South Korea, Sri Lanka, Malaysia, Mexico, New Zealand, Peru, Philippines, Singapore, Russia, Thailand, Vietnam, and South Africa that are directed to low dose compositions and rapid onset methods of using MIN-117 to treat depression without cognition impairment.

If granted, the patent terms of these applications expire no earlier than January 24, 2034. Patent term extensions of up to five years may be available in the United States.

MIN-117 Patents and Applications Licensed to Us

Our MIN-117 patent portfolio also consists of licensed patent rights. We are the exclusive licensee of patents in the United States, Europe and Canada which claim pharmaceutical compositions and uses of MIN-117 to treat depression. The European patent is validated in Germany, Spain, France, Italy, the Netherlands, and the United Kingdom.

As part of the license agreement, Minerva has the right to develop, sell, and import products related to MIN-117 in the rest of the world, except in MTPC territories which include the Asia-Pacific region and specifically consists of the countries of Bangladesh, Brunei, India, Indonesia, Japan, Malaysia, Pakistan, the People's Republic of China (including Hong Kong), Philippines, Singapore, South Korea, Sri Lanka, Taiwan, Thailand, and Vietnam.

The foreign patents expire no earlier than May 22, 2020. The U.S. '320 patent expires no earlier than August 13, 2020.

Ongoing development and clinical trials may lead to additional patent filings directed to MIN-117.

MIN-202

Our MIN-202 patent portfolio consists of patent rights licensed from Janssen Pharmaceutica NV. We are the exclusive licensee of European Patent Application EP 2491038 A1, which claims a genus of compositions of matter that encompasses MIN-202 and other orexin receptor modulators, and methods of using these compositions to treat diseases, including diseases mediated by orexin receptor activity.

If granted, the patent term of this application expires no earlier than October 21, 2030.

MIN-301

Our MIN-301 patent portfolio includes two families of patents and patent applications directed to MIN-301 and its use in the treatment of neurologic and psychiatric diseases. The MIN-301 portfolio was assigned to Mind-NRG by ProteoSys, Inc.

The first family is directed to the medical use of a specific neuregulin isoform as well as compositions comprising said neuregulin isoform and a further medicament.

This patent family includes patents granted in Europe, Australia, Russia and Japan and patent applications pending in the United States, Japan, Brazil, Canada, Mexico and China. The European patent was validated in Austria, Switzerland, Germany, Denmark, Spain, France, United Kingdom, Greece, Ireland, Italy, Netherlands, Norway, Portugal, Sweden, Belgium and Turkey.

The patent term of the first family will expire no earlier than November 17, 2028. Patent term extensions of up to five years may be available in the United States.

The second family includes applications pending in the United States and the PCT is directed to MIN-301 compositions and an analogue and methods for treating Parkinson's disease.

If granted, the patent terms are expected to expire no earlier than January 5, 2036. Patent term extensions of up to five years may be available in the United States.

Ongoing development and clinical trials may lead to additional patent filings. The patent term is 20 years from the earliest effective filing date subject to any disclaimers or extensions. In addition, the term of a patent in the United States can be adjusted and extended due to delays in the patent examination process by the United States Patent and Trademark Office. In the United States, the patent term of a patent that covers an FDA-approved drug that contains an active ingredient or salt or ester of the active ingredient that has not previously been marketed may also be eligible for patent term extension, which permits patent term restoration to account for a portion of the patent term lost during the FDA regulatory review process.

Manufacturing

We do not have any manufacturing facilities or personnel. We currently rely, and expect to continue to rely, on third parties for the manufacturing of our product candidates for pre-clinical and clinical testing, as well as for commercial manufacturing if our product candidates receive marketing approval. Our product candidates are manufactured in reliable and reproducible synthetic processes from readily available starting materials. The chemistry does not require unusual equipment in the manufacturing process. We expect to continue to develop product candidates that can be produced cost-effectively at contract manufacturing facilities.

Commercialization

We have not yet established a sales, marketing or product distribution infrastructure. We have global, except for most of Asia, commercialization rights for two of our product candidates, MIN-101 and MIN-117, and European Union commercialization rights for MIN-202. We have worldwide rights for MIN-301. We believe that it will be possible for us to access European and, in the case of MIN-101, MIN-117 and MIN-301, the United States and Latin America markets through a focused, specialized task force where the population dynamics would prove efficient. Alternatively, we may enter into distribution and other marketing arrangements with third parties for any of our drug candidates that obtain marketing approval.

Subject to receiving marketing approvals, we expect to commence commercialization activities by building a focused sales and marketing organization, either alone or through collaborations with third parties, in the United States, EU and Latin America to sell our product candidates. We believe that such an organization will be able to target the community of physicians who are the key specialists in treating the patient populations for which our product candidates are being developed.

We plan to build a marketing and sales management organization to create and implement marketing strategies for any products we commercialize ourselves. In parallel with building this organization, we plan to develop educational initiatives with respect to approved products and relationships with thought leaders in relevant fields of medicine. As part of our commitment to supporting optimal patient care and sustainable healthcare systems globally, we recognize the importance of fully understanding the needs of the patient communities we serve. We have learned that one of the best ways to accomplish this is by working with patient organizations, who are closely connected to patients' most important concerns and interests.

Government Regulation and Product Approval

Clinical Trials and Marketing Authorization in the European Union

In Europe, a clinical trial application, or CTA, must be submitted to the competent national regulatory authority and to independent ethics committees in each country in which we intend to conduct clinical trials. Once the CTA is approved in accordance with that country's requirements, clinical trial development may proceed in that country. In all cases, the clinical trials must be conducted in accordance with good clinical practices and other applicable regulatory requirements. A clinical trial may only be undertaken subject to certain conditions. The relevant ethics committee must give its opinion, before a clinical trial commences, on any issue requested. Clinical trials information must be entered into a European database. There are strict requirements in relation to the labeling and packaging of our product candidates, the verification of compliance with the provisions on good clinical and manufacturing practice and the notification of adverse events and serious adverse reactions.

Under European Union regulatory systems, a company may not market a medicinal product without marketing authorization.

There are four procedures for submitting a Marketing Authorization Application, or MAA, in the EU: (i) the national procedure, (ii) the mutual recognition procedure, or MRP; (iii) the decentralized, or DCP and (iv) the centralized procedure, or CP. The submission strategy for a given product will depend on the nature of the product, the target indication(s), the history of the product, and the marketing plan. The centralized procedure is compulsory for certain medicinal products which are produced by biotechnology processes, advanced therapy medicinal products and orphans. Besides the products falling under the mandatory scope, the centralized procedure is also open for medicinal products that constitute a significant therapeutic, scientific or technical innovation i.e. new active substances or other medicinal products that constitute a significant therapeutic, scientific or technical innovation.

The centralized procedure leads to approval of the product in all 28 EU member states and in Norway, Iceland and Liechtenstein. Submission of one MAA thus leads to one assessment process and one authorization that allows access to the market of the entire EU. The process of the centralized procedure is triggered when the applicant submits an MAA to the EMA. The letter of intent also initiates the assignment of the Rapporteur and Co-Rapporteur, who are the two appointed members of the Committee for Human Medicinal Products, or CHMP, representing two EU member states.

When using the MRP or DCP, the applicant must select which and how many EU member states in which to seek approval. In the case of an MRP, the applicant must initially receive national approval in one EU member state. This will be the so-called reference member state, or RMS, for the MRP. Then, the applicant seeks approval for the product in other EU member states, the so-called concerned member states, or CMS, in a second step: the mutual recognition process. For the DCP, the applicant will approach all chosen member states at the same time. To do so, the applicant will identify the RMS that will assess the submitted MAA and provide the other selected member states with the conclusions und results of the assessment.

However an innovator company enjoys a period of “data exclusivity” during which their pre-clinical and clinical trials data may not be referenced in the regulatory filings of another company (typically a generic company) for the same drug substance.

Data exclusivity in Europe is 8 years from the date of first authorization in Europe with an additional period of 2 years of "market exclusivity." This is the period of time during which a generic company may not market an equivalent generic version of the originator's pharmaceutical product. An additional 1 year may be obtained in where the innovator company is granted a marketing authorization within the above 8-year period for a significant new indication for the relevant medicinal product.

The Pediatric Regulation provides that an application for a new marketing authorization must include the results of all trials performed and details of all information collected in compliance with an agreed pediatric investigation plan, or PIP, unless a specific exemption is granted on the basis that pediatric use is not relevant - also the requirement can be deferred by agreement.

When the application for marketing authorization is made, the competent authority responsible for granting a marketing authorization must verify whether the application complies with the relevant requirements, including compliance with the agreed PIP. Assuming it does, the marketing authorization may be granted and the relevant results are included in the summary of product characteristics, or SmPC, for the product, along with a statement indicating compliance with the agreed PIP. The applicant then receives the six month extension to the SPC. It is not necessary for the product actually to be indicated for use in the pediatric population (for example, if the results show that that would not be appropriate).

U.S. FDA Approval Process

In the United States, pharmaceutical products are subject to extensive regulation by the FDA. The Federal Food, Drug, and Cosmetic Act, or the FDCA, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, packaging, storage, recordkeeping, approval, labeling, advertising, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve pending Investigational New Drug Applications, or INDs, and NDAs, withdrawal of a marketing approval, imposition of clinical holds or termination of clinical trials, or issuance of Warning, Cyber, or Untitled Letters, product recalls, product seizures, refusal to allow imports or exports total or partial suspension of production or distribution, debarment, injunctions, fines, refusal of government contracts, exclusion from participation in federal and state healthcare programs, restitution, disgorgement, civil penalties and criminal prosecution, including criminal fines and imprisonment.

FDA approval is required before any new unapproved drug or dosage form, including a new use of a previously approved drug, can be marketed in the United States. Pharmaceutical product development in the United States typically involves, among other things, pre-clinical laboratory and animal tests, the submission to the FDA of an IND, which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and effectiveness of the drug for each indication for which FDA approval is sought. Satisfaction of FDA pre-market approval requirements typically takes many years and significant financial investment, and the actual time and cost required may vary substantially based upon the type, complexity and novelty of the product or disease indicated for treatment.

Pre-clinical tests include laboratory evaluation of product chemistry, pharmacology, stability, formulation and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements including good laboratory practices. The results of pre-clinical testing are submitted to the FDA as part of an IND along with other information including information about product chemistry, manufacturing and controls, any available clinical data or literature, and a proposed clinical trial protocol, among other items. Certain pre-clinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may be conducted after the IND is submitted. A 30-day waiting period after

the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has not placed a clinical hold on the IND within this 30-day period, the clinical trial proposed in the IND may begin. Should FDA place a clinical hold on the IND, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial may begin.

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of a qualified investigator. Clinical trials must be conducted in compliance with federal regulations, good clinical practices, or GCP, which include the ethical principles that all research subjects provide their informed consent in writing for their participation in any clinical trial, and that all trials be approved and monitored on an ongoing basis by an institutional review board, or IRB. Clinical trials must also be conducted under protocols detailing the objectives of the trial, trial procedures, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated, and a statistical analysis plan. Each protocol involving testing in U.S. subjects and subsequent protocol amendments must be submitted to the FDA as part of the IND. The study protocol and informed consent information for subjects in clinical trials, along with all amendments, must also be submitted to an IRB for approval.

Clinical trials to support NDAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase I, the initial introduction of the drug into healthy human subjects or subjects with the target disease or condition, the drug is tested to assess safety, metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses and, if possible, early evidence of effectiveness. Phase II usually involves trials in a limited subject population with the target disease or

condition to evaluate the effectiveness of the drug for a particular indication or indications, dosage tolerance and optimum dosage, and identify possible adverse effects and safety risks. If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase II evaluations, generally two adequate and well-controlled Phase III trials are undertaken to obtain additional information about clinical efficacy and safety in a larger number of subjects, typically at geographically dispersed clinical trial sites, to establish the overall benefit-risk relationship of the drug and to provide adequate information for the labeling of the drug. In some cases, the FDA may condition approval on the sponsor's agreement to conduct additional clinical trials to further assess the drug's safety and effectiveness after approval. Such post-approval trials are typically referred to as Phase IV trials. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Information about certain clinical trials, including a description of the study and study results must also be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on their clinicaltrials.gov website.

The manufacture of investigational drugs for the conduct of human clinical trials is subject to the Current Good Manufacturing Practices, or cGMPs. Investigational drugs and active pharmaceutical ingredients, imported into the United States are also subject to regulation by FDA relating to their labeling and distribution. Further, the export of investigational drug products outside of the United States is subject to regulatory requirements of the receiving country as well as United States export requirements.

The FDA may suspend or terminate a clinical trial, or impose other sanctions, at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk or if it believes that the clinical trials are not being conducted in accordance with FDA requirements. 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 subjects, or may impose other conditions on the conduct of the research. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group regularly reviews accumulated data and advises the study sponsor regarding the continuing safety of trial subjects, potential trial subjects, and the continuing validity and scientific merit of the clinical trial. Sponsors may also suspend or terminate a clinical trial based on safety concerns, a lack of evidence of drug efficacy, evolving business objectives and/or competitive climate.

After completion of the required clinical testing, an NDA is prepared and submitted to the FDA. FDA approval of the NDA is required before marketing of the product may begin in the United States. The NDA must include the results of all pre-clinical, clinical and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture and controls, and proposed labeling, among other things. Under federal law, the submission of most marketing applications is subject to a substantial application user fee, and the manufacturer and/or sponsor under an approved application are also subject to annual product and establishment fees.

In addition, under the Pediatric Research Equity Act, or PREA, a marketing application or supplement to a marketing application for a new active ingredient, indication, dosage form, dosage regimen or route of administration must contain data that are adequate 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, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

The FDA also may require submission of a risk evaluation and mitigation strategy, or REMS, either during the application process or after the approval of the drug to mitigate any identified or suspected serious risks, and to

identify any new risks that were not apparent in clinical investigations. The REMS plan could include medication guides, physician communication plans, assessment plans, and elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

Under the Prescription Drug User Fee Act the FDA has agreed to certain performance goals in the review of NDAs. The FDA has a goal of reviewing ninety percent of applications for non-priority drug products within 10 months of the FDA's acceptance of the full application for filing. The review process may be extended by the FDA under certain circumstances.

Under the FDCA and FDA guidance, before approving a drug for which no active ingredient (including any ester or salt of the active ingredients) has previously been approved by the FDA or a first-of-a-kind, first-in-class biologic, FDA must either refer that drug to an external advisory committee or provide in an action letter, a summary of the reasons why FDA did not refer the drug to an advisory committee. The external advisory committee review may also be required for other drugs because of certain other issues, including

clinical trial design, safety and effectiveness, and public health questions. An advisory committee is a panel of independent experts, including clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Additionally, the FDA will inspect the facility or the facilities at which the drug is manufactured. The FDA will not approve the product unless the facility, and all of its subcontractors and contract manufacturers, demonstrate compliance with cGMPs, and provide adequate assurance that they can consistently produce the product within required specifications, and the NDA contains data that provides substantial evidence that the drug is safe and effective for the indication sought in the proposed labeling. Additionally, the FDA will typically inspect one or more clinical trial sites to assure compliance with GCPs before approving a marketing application. After the FDA evaluates the marketing application and the manufacturing facilities, it may issue an approval letter, or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA may issue an approval letter.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy and may impose other conditions, including labeling restrictions, limitations on the approved indications, contraindications, warnings or precautions, such as black boxed warnings, distribution restrictions or other risk-management mechanisms under a REMS which can materially affect the potential market and profitability of the drug. The FDA may prevent or limit further marketing of a product based on the results of post-marketing trials or surveillance programs. Further, if there are any modifications to the drug, including changes in indications, labeling, manufacturing processes or facilities, or new safety issues arise, a new or supplemental NDA or a post-implementation notification or other report may be required or requested depending on the change, which may require additional data or additional pre-clinical studies and clinical trials. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion, and reporting of adverse experiences with the product and drug shortages. After approval, most changes to the approved product, such as adding new indications, manufacturing changes or other labeling claims, are subject to further testing requirements and prior FDA review and approval.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are subject to periodic announced and unannounced inspections by the FDA and these state agencies for compliance with cGMP and other regulatory requirements. Changes to the manufacturing process are strictly regulated and may require prior FDA approval or notification before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market trials or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, Untitled Letters, Warning Letters, Cyber Letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of administrative civil or criminal penalties, including fines and imprisonment.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Although physicians, in the practice of medicine, may prescribe approved drugs for unapproved indications if in their professional medical judgment they believe it to be appropriate, pharmaceutical companies may only market and promote their drug products for the FDA approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws prohibiting the marketing and promotion of off-label uses, and a company that is found to have improperly marketed or promoted off-label uses may be subject to significant liability, including, among others, criminal and civil penalties under the FDCA and False Claims Act, exclusion from participation in federal healthcare programs, and mandatory compliance programs.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Moreover, the recently enacted Drug Quality and Security Act imposes new obligations on manufacturers of pharmaceutical products, among others, related to product and tracking and tracing.

Federal and State Fraud and Abuse, Data Privacy and Security and Transparency Laws

In addition to FDA restrictions on marketing and promotion of pharmaceutical products, other federal and state healthcare laws restrict business practices in the biopharmaceutical industry. These laws include, without limitation, state and federal anti-kickback and false claims laws, data privacy and security laws, as well as transparency laws regarding payments or other items of value provided to healthcare providers. Applicable state anti-kickback and false claims laws may be broader in scope than federal law and may apply regardless of payor, in addition to items and services reimbursed under Medicaid and other state programs.

We may also be subject to state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. In addition, we may be subject to reporting requirements under state transparency laws, as well as state laws that require pharmaceutical companies to comply with the industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government that otherwise restricts certain payments that may be made to healthcare providers and entities.

If our operations are found to be in violation of any of the health regulatory laws described above or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal and civil and/or administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government healthcare programs, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our products are sold in a foreign country, we may be subject to similar foreign laws.

Coverage and Reimbursement

The commercial success of our product candidates and our ability to commercialize any approved product candidates successfully will depend in part on the extent to which governmental authorities, private health insurers and other third-party payors provide coverage for and establish adequate reimbursement levels for our product candidates, once approved.

Government health administration authorities, private health insurers and other third-party payors generally decide which drugs they will pay for and establish reimbursement levels for healthcare. In particular, in the United States, private health insurers and other third-party payors often provide reimbursement for products and services based on the level at which the government (through the Medicare or Medicaid programs) provides reimbursement for such treatments. Sales of our product candidates will therefore depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be covered by third-party payors. The market for our product candidates will depend significantly on access to third-party payors' formularies without prior authorization, step therapy, or other limitations such as approved lists of treatments for which third-party payors provide coverage and reimbursement. Also, third-party payors are developing increasingly sophisticated methods of controlling healthcare costs. Coverage and reimbursement for therapeutic products can differ significantly from payor to payor. A third-party payors' decision to provide coverage for a medical product or service does not imply that an adequate reimbursement rate will be approved. One third-party payor's decision to cover a particular medical product or service does not ensure that other payors will also provide coverage for the medical product or service, or will provide coverage at an adequate reimbursement rate. As a result, the coverage determination process will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that adequate coverage and reimbursement will be obtained.

In the United States, the European Union and other potentially significant markets for our product candidates, government authorities and other third-party payors are developing increasingly sophisticated methods of controlling healthcare costs and are increasingly imposing additional requirements and restrictions on coverage.

Further, the increased emphasis on managed healthcare in the United States and on country and regional pricing and reimbursement controls in the European Union will put additional pressure on product pricing, reimbursement and utilization, which may adversely affect our future product sales and results of operations. These pressures can arise from rules and practices of managed care organizations, competition within therapeutic classes, availability of generic equivalents or biosimilars, judicial decisions and governmental laws related to Medicare, Medicaid and healthcare reform, pharmaceutical coverage and reimbursement policies and pricing in general. The cost containment measures that healthcare payors and providers are instituting and the effect of any healthcare reform implemented in the future could significantly reduce our revenues from the sale of any approved product candidates. We cannot provide any assurances that we will be able to obtain and maintain governmental or private third-party coverage or adequate reimbursement for our product candidates in whole or in part. Additionally, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs.

Healthcare Reform

The United States and some foreign jurisdictions are considering enacting or have enacted a number of additional legislative and regulatory proposals designed to change the healthcare system in ways that could affect our ability to sell our products profitably.

In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives, including the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, PPACA), which substantially changed healthcare financing and delivery by both governmental and private insurers, and significantly impact the pharmaceutical industry. Among other things, PPACA expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program. This could increase the amount of Medicaid drug rebates manufacturers are required to pay to states. The legislation also extended Medicaid drug rebates, previously due only on fee-for-service utilization, to Medicaid managed care utilization, and created an alternate rebate formula for new formulations of certain existing products. PPACA also expanded the types of entities eligible for the 340B drug discount program that mandates discounts to certain hospitals, community centers and other qualifying providers. Further, PPACA established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D. Finally, PPACA establishes an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents and expands Medicaid benefits. There have been judicial and Congressional challenges to certain aspects of PPACA, and we expect there will be additional challenges and amendments to PPACA in the future.

In addition, other legislative changes have been proposed and adopted since PPACA was enacted. For example, in August 2011, the President signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reduction to several government programs. This included reductions to Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013, following passage of the Bipartisan Budget Act of 2015, and will stay in effect through 2025 unless additional Congressional action is taken. Additionally,

in January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals and imaging centers. Further, in January 2016, the Centers for Medicare and Medicaid Services issued a final rule regarding the Medicaid drug rebate program. The final rule, effective April 1, 2016, among other things, revises the manner in which the "average manufacturer price" is to be calculated by manufacturers participating in the program and implements certain amendments to the Medicaid rebate statute created under PPACA.

The Foreign Corrupt Practices Act

The Foreign Corrupt Practices Act, or the FCPA, prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. Activities that violate the FCPA, even if they occur wholly outside the United States, can result in criminal and civil fines, imprisonment, disgorgement, oversight, and debarment from government contracts.

Regulation of Biologics

One of our product candidates, MIN-301, is a peptide, and, as such, will likely be considered to be a biologic by the FDA. Biologics are regulated under the PHSA and FDCA. Because biologics also meet the FDCA's definition of a drug, many aspects of the FDA's regulation of biologics are the same as or similar to drugs, though there are some differences. As with drugs, a product sponsor must conduct pre-clinical testing, obtain an IND for the conduct of clinical studies, and conduct clinical trials in accordance with FDA's requirements to support a marketing application. Following completion of clinical testing, however, the product sponsor usually will be required to submit a BLA to FDA. Rather than demonstrating safety and efficacy, as in the case of an NDA, a BLA must demonstrate that the biologic is safe, pure and potent. Accordingly, different information must be included in the BLA to meet the FDA's approval standards. Similarly, following product approval, biologics are subject to many of the same regulatory requirements as drugs, including requirements pertaining to record keeping, periodic reporting, distribution, labeling, post-approval trials, REMS, advertising and promotion, reporting of adverse experiences and product shortages, and the manufacture of products in accordance with cGMPs. Unlike drugs, biologics are also subject to lot-release requirements, which require submission of product samples and testing information to the FDA. The products may not be distributed until the lot is released by the FDA. Biologics are further subject to the same fraud and abuse, data privacy, security, and transparency laws as drugs. Generally, brand biologics are covered and reimbursed by government and commercial health plans as single-source drugs.

Employees

As of December 31, 2015, we had 9 full-time employees. In addition, we are or have engaged with a number of consultants and companies, including Pharma Partnering in Research & Strategy SAS, or PPRS, that provide expertise in the key functions involved with the development of our products. None of our employees is subject to a collective bargaining agreement and we consider our relationship with our employees to be good.

Available Information

We file reports with the Securities and Exchange Commission, or SEC, including annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K any other filings required by the SEC. We make available on our website (www.minervaneurosciences.com) our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and all amendments to those reports as soon as reasonably practicable after such material is electronically filed with or furnished to the SEC. These materials are available free of charge on or through our website via the Investor Relations page at www.minervaneurosciences.com. References to our website address in this report are intended to be inactive textual references only, and none of the information contained on our website is part of this report or incorporated in this report by reference.

The public may read and copy any materials we file with the SEC at the SEC's Public Reference Room at 100 F Street, NE, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet site (http://www.sec.gov) that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC.

ITEM 1A. Risk Factors

This Annual Report on Form 10-K contains forward-looking information based on our current expectations. Because our actual results may differ materially from any forward-looking statements that we make or that are made on our

behalf, this section includes a discussion of important factors that could affect our actual future results, including, but not limited to, our capital resources, the progress and timing of our clinical programs, the safety and efficacy of our product candidates, risks associated with regulatory filings, risks associated with determinations made by regulatory agencies, the potential clinical benefits and market potential of our product candidates, commercial market estimates, future development efforts, patent protection, effects of healthcare reform, reliance on third parties, and other risks set forth below.

Risks Related to Our Financial Position and Capital Requirements

We have incurred significant losses since our inception. We expect to continue to incur losses over the next several years and may never achieve or maintain profitability.

We are a clinical development-stage biopharmaceutical company. In November 2013, we merged with Sonkei Pharmaceuticals, Inc., or Sonkei, and, in February 2014, we acquired Mind-NRG, which were also clinical development-stage biopharmaceutical companies. Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain regulatory approval or become commercially viable. As an early stage company, we have limited experience and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and

rapidly evolving fields, particularly the biopharmaceutical area. We have no products approved for commercial sale and have not generated any revenue from product sales to date, and we continue to incur significant research and development and other expenses related to our ongoing operations.

We are not profitable and have incurred losses in each period since our inception in 2007. For the years ended December 31, 2015, and 2014, we reported net losses of $27.1 million and $56.9 million, respectively. As of December 31, 2015, we had an accumulated deficit of $101.8 million.

We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our research and development of, and seek regulatory approvals for, our product candidates. If any of our product candidates fail in clinical trials or do not gain regulatory approval, or if any of our product candidates, if approved, fail to achieve market acceptance, we may never generate revenue or become profitable. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

We will require additional capital to finance our operations, which may not be available to us on acceptable terms, or at all. As a result, we may not complete the development and commercialization of our product candidates or develop new product candidates.

Our operations and the historic operations of Sonkei and Mind-NRG have consumed substantial amounts of cash since inception. We expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we advance our product candidates into clinical trials.

As of December 31, 2015, we had cash, cash equivalents and marketable securities of $32.2 million. We believe that our cash, cash equivalents and marketable securities as of December 31, 2015, together with the approximately $17.5 million in gross proceeds received from the exercise of warrants subsequent to December 31, 2015 and described elsewhere in this Annual Report, will fund our projected operating requirements into the second quarter of 2017. In particular, we expect these funds will allow us to complete our Phase IIb trial for MIN-101, our Phase IIa trial for MIN-117, our portion of the funding for the Phase IIa trial in primary insomnia for MIN-202 with Janssen, our portion of the funding for the Phase Ib trial in comorbid insomnia for MIN-202 with Janssen and additional pre-clinical development for MIN-301. However, circumstances may cause us to consume capital more rapidly than we currently anticipate. In any event, we will require significant additional capital to fund future clinical trials of our product candidates, and to obtain regulatory approval for, and to commercialize, our product candidates.

Our future funding requirements, both short and long-term, will depend on many factors, including:

- the initiation, progress, timing, costs and results of pre-clinical studies and clinical trials for our product candidates and future product candidates we may develop;
- the outcome, timing and cost of seeking and obtaining regulatory approvals from the EMA, FDA, and comparable foreign regulatory authorities, including the potential for such authorities to require that we perform more studies than those that we currently expect;
- the cost to establish, maintain, expand and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with licensing, preparing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights;
- the effect of competing technological and market developments;
- market acceptance of any approved product candidates;

- the costs of acquiring, licensing or investing in additional businesses, products, product candidates and technologies; and
- the cost of establishing sales, marketing and distribution capabilities for our product candidates for which we may receive regulatory approval and that we determine to commercialize ourselves or in collaboration with our partners.

When we need to secure additional financing, such additional fundraising efforts may divert our management from our day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. If we raise additional equity financing, our stockholders may experience significant dilution of their ownership interests, and the per-share value of our common stock could decline. If we engage in debt financing, we may be required to accept terms that restrict our ability to incur additional indebtedness and force us to maintain specified liquidity or other ratios. Further, the evolving and volatile global economic climate and global financial market conditions could limit our ability to raise funding and otherwise adversely impact our business or those of our collaborators and providers. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us

we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our product candidates. Any of these events could significantly harm our business, financial condition and prospects.

Changes in estimates regarding fair value of intangible assets may result in an adverse impact on our results of operations.

We test goodwill and in-process research and development for impairment annually or more frequently if changes in circumstances or the occurrence of events suggest impairment exists. The test for impairment of in-process research and development requires us to make several estimates about fair value, most of which are based on projected future cash flows. Changes in these estimates may result in the recognition of an impairment loss in our results of operations. An impairment analysis is performed whenever events or changes in circumstances indicate that the carrying amount of any individual asset may not be recoverable. For example, if we or our counterparties fail to perform our respective obligations under an agreement, or if we lack sufficient funding to develop our product candidates, an impairment may result. In addition, any significant change in market conditions, estimates or judgments used to determine expected future cash flows that indicate a reduction in carrying value may give rise to impairment in the period that the change becomes known.

We plan to use potential future operating losses and our federal and state net operating loss, or NOL, carryforwards to offset taxable income from revenue generated from operations or corporate collaborations. However, our ability to use existing NOL carryforwards may be limited as a result of issuance of equity securities.

As of December 31, 2015, we had approximately $36.1 million of Federal NOL carryforwards. These Federal NOL carryforwards will begin to expire at various dates beginning in 2027, if not utilized. We plan to use our operating losses to offset any potential future taxable income generated from operations or collaborations. To the extent we generate taxable income, we plan to use our existing NOL carryforwards and future losses to offset income that would otherwise be taxable. However, under the Tax Reform Act of 1986, the amount of benefits from our NOL carryforwards may be impaired or limited if we incur a cumulative ownership change of more than 50%, as interpreted by the U.S. Internal Revenue Service, over a three year period. We have not performed a detailed analysis to determine whether an ownership change occurred upon consummation of the merger between us and Sonkei, upon the acquisition of Mind-NRG or our initial public offering or the concurrent private placements. However, as a result of these transactions, it is likely that an ownership change has occurred. Therefore, it is likely that some or all of our existing NOL carryforwards would be limited by the provisions of Section 382 of the United States Internal Revenue Code of 1986, as amended. Further, state NOL carryforwards may be similarly limited. We had approximately $28.4 million of state net operating carryforwards at December 31, 2015. It is also possible that future changes in ownership, including as a result of subsequent sales of securities by us or our stockholders, could similarly limit our ability to utilize NOL carryforwards. It is possible that all of our existing NOL carryforwards have been or will be disallowed. Any such disallowances may result in greater tax liabilities than we would incur in the absence of such a limitation and any increased liabilities could adversely affect our business, results of operations, financial condition and cash flow.

Risks Related to Our Business and Industry

We cannot give any assurance that any of our product candidates will receive regulatory approval in a timely manner or at all, which is necessary before they can be commercialized.

The regulatory approval process is expensive and the time required to obtain approval from the EMA, FDA or other regulatory authorities in other jurisdictions to sell any product is uncertain and may take years.

Whether regulatory approval will be granted is unpredictable and depends upon numerous factors, including the substantial discretion of the regulatory authorities. Moreover, the filing of a marketing application, including a New Drug Application, or NDA, requires a payment of a significant user fee upon submission. The filing of marketing applications for our product candidates may be delayed due to our lack of financial resources to pay such user fee.

If, following submission, our NDA or marketing authorization application is not accepted for substantive review or approval, the EMA, FDA or other comparable foreign regulatory authorities may require that we conduct additional clinical or pre-clinical trials, provide additional data, manufacture additional validation batches or develop additional analytical tests methods before they will reconsider our application. If the EMA, FDA or other comparable foreign regulatory authorities requires additional studies or data, we would incur increased costs and delays in the marketing approval process, which may require us to expend more resources than we have available. In addition, the EMA, FDA or other comparable foreign regulatory authorities may not consider sufficient any additional required trials, data or information that we perform or provide, or we may decide, or be required, to abandon the program.

Moreover, policies, regulations, or the type and amount of pre-clinical and clinical data necessary to gain approval may change during the course of a product candidate’s clinical development and may vary among jurisdictions. It is possible that none of our existing product candidates or any of our future product candidates will ever obtain regulatory approval, even if we expend substantial time and resources seeking such approval.

Our product candidates could fail to receive regulatory approval for many reasons, including the following:

- The EMA, FDA or other regulatory authorities may disagree with the design or implementation of our clinical trials. We have not yet consulted with the EMA or the FDA on the design and conduct of the clinical trials that have already been conducted or that we intend to conduct. Thus, the EMA, FDA and other comparable foreign authorities may not agree with the design or implementation of these trials. We intend to seek guidance from the EMA in relation to the European Union clinical trial program and the FDA on the design and conduct of clinical trials of our compounds when we initiate a clinical program in the United States in the future.
- We may be unable to demonstrate to the satisfaction of the EMA, FDA or other regulatory authorities that a product candidate is safe and effective for its proposed indication.
- The results of clinical trials may not meet the level of statistical significance required by the EMA, FDA or other regulatory authorities for approval.
- We may be unable to demonstrate that a product candidate's clinical and other benefits outweigh any safety risks.
- The EMA, FDA or other regulatory authorities may disagree with our interpretation of data from pre-clinical studies or clinical trials.
- The data collected from clinical trials of our product candidates may not be sufficient to support an NDA or other submission or to obtain regulatory approval in the United States or elsewhere.
- The EMA, FDA or other regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies.
- The approval policies or regulations of the EMA, FDA or other regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Even if we obtain approval for a particular product, regulatory authorities may approve that product for fewer or more limited indications, including more limited patient populations, than we request, may require that contraindications, warnings, or precautions be included in the product labeling, including a black box warning, may grant approval contingent on the performance of costly post-marketing clinical trials or other post-market requirements, including risk evaluation and mitigation strategies, or REMS, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product. Any of the foregoing could materially harm the commercial prospects for our product candidates.

Results of earlier clinical trials may not be predictive of the results of later-stage clinical trials.

The results of pre-clinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Interpretation of results from early, usually smaller, trials that suggest positive trends in some subjects, require caution. Results from later stages of clinical trials enrolling more subjects may fail to show the desired safety and efficacy results or otherwise fail to be consistent with the results of earlier trials of the same product candidate. This may occur for a variety of reasons, including differences in trial design, trial endpoints (or lack of trial endpoints in exploratory studies), subject population, number of subjects, subject selection criteria, trial duration, drug dosage and formulation or due to the lack of statistical power in the earlier trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety profiles, notwithstanding promising results in earlier trials.

The results of clinical trials conducted at sites outside the United States may not be accepted by the FDA and the results of clinical trials conducted at sites in the United States may not be accepted by international regulatory authorities.

We plan to conduct our clinical trials outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of this data would be subject to certain conditions imposed by the FDA. For example, the clinical trial must be well-designed and conducted and performed by qualified investigators in accordance with ethical safeguards such as institutional review board, or IRB, or ethics committee approval and

informed consent. The study population must also adequately represent the applicable United States population, and the data must be applicable to the American population and medical practice in ways that the FDA deems clinically meaningful. In addition, while clinical trials conducted outside of the United States are subject to the applicable local laws, FDA acceptance of the data from such trials will be dependent upon its determination that the trials were conducted consistent with all applicable United States laws and regulations. There can be no assurance the FDA will accept data from trials conducted outside of the United States as adequate support of a marketing application, and it is not unusual for the FDA to require some Phase III clinical trial data to be generated in the United States. If the FDA does not accept the data from our international clinical trials, it would likely result in the need for additional trials in the United States, which would be costly and time-consuming and could delay or permanently halt the development of one or more of our product candidates.

If we experience delays in clinical testing, we will be delayed in commercializing our product candidates, our costs may increase and our business may be harmed.

We do not know whether our clinical trials will be completed on schedule, or at all. Our product development costs will increase if we experience delays in clinical testing. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which would impair our ability to successfully commercialize our product candidates and may harm our business, results of operations and prospects.

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, which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- deviations from the trial protocol by clinical trial sites and investigators, or failing to conduct the trial in accordance with regulatory requirements;
- failure of our third parties, such as CROs, to satisfy their contractual duties or meet expected deadlines;
    - insufficient or inadequate supply or quantity of product material for use in trials due to delays in the importation and manufacture of clinical supply, including delays in the testing, validation, and delivery of the clinical supply of the investigational drug to the clinical trial sites;
- delays in identification and auditing of central or other laboratories and the transfer and validation of assays or tests to be used;
- delays in having subjects complete participation in a trial or return for post-treatment follow-up;
- difficulties obtaining IRB or ethics committee approval to conduct a trial at a prospective site, or complying with conditions imposed by IRBs or ethics committees;
- challenges recruiting and enrolling subjects 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 adverse events experienced by subjects in a clinical trial;
- difficulty retaining subjects 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, which are common among schizophrenia and MDD subjects who we require for our clinical trials of two of our product candidates, MIN-101 and MIN-117;
- delays in adding new investigators and clinical sites;
- withdrawal of clinical trial sites from clinical trials;
- lack of adequate funding; and
- clinical holds or termination imposed by the European Union national regulatory authorities, the FDA or IRBs or ethics committees.

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 European Union national regulatory authorities or the FDA due to a number of factors, including:

- failure to conduct the clinical trial in accordance with regulatory requirements, the trial protocols and applicable laws;
- observations during inspection of the clinical trial operations or trial sites by the EMA, FDA or other comparable foreign regulatory authorities that ultimately result in the imposition of a clinical hold;
- unforeseen safety issues; or

· lack of adequate funding to continue the clinical trial.

Failure to conduct a clinical trial in accordance with regulatory requirements, the trial protocols and applicable laws may also result in the inability to use the data from such trial to support product approval. 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 the EMA, FDA, IRBs or ethics committees for reexamination, which may impact the costs, timing and successful completion of a clinical trial. Many of the factors that cause, or lead to, a delay in the commencement or completion of a clinical trial may also ultimately lead to the denial of regulatory approval of the associated product candidate. 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 have no experience in advancing product candidates beyond Phase II, which makes it difficult to assess our ability to develop and commercialize our product candidates.

We have no experience in progressing clinical trials past Phase II, obtaining regulatory marketing approvals or commercializing product candidates. We merged with Sonkei and acquired Mind-NRG and have limited operating history since the respective merger and acquisition. We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in pursuing our business objectives. We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

If we are unable to enroll subjects in clinical trials, we will be unable to complete these trials on a timely basis or at all.

The timely completion of clinical trials largely depends on subject enrollment. Many factors affect subject enrollment, including:

- the size and nature of the subject population;
- the number and location of clinical sites we enroll;
- competition with other companies for clinical sites or subjects;
- the eligibility and exclusion criteria for the trial;
- the design of the clinical trial;
- inability to obtain and maintain subject consents;
- risk that enrolled subjects will drop out before completion; and
- clinicians' and subjects' perceptions as to the potential advantages or disadvantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

We rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials in Europe and, we expect, eventually in the United States and, while we have agreements governing their committed activities, we have limited influence over their actual performance. We may also experience difficulties enrolling subjects for our clinical trials relating to MIN-101 and MIN-117 due to the mental health of the subjects that we will need to enroll, related diagnoses and drop-out rates.

Our clinical trials may fail to demonstrate adequately the safety and efficacy of our product candidates, which could prevent or delay regulatory approval and commercialization, and also increase costs.

Before obtaining regulatory approvals for the commercial sale of our product candidates, we must demonstrate through lengthy, complex and expensive pre-clinical testing and clinical trials that our product candidates are both safe and effective for use in each target indication, and failures can occur at any stage of testing. Clinical trials often fail to demonstrate safety and efficacy of the product candidate studied for the target indication. For instance, our clinical trials of MIN-101 and MIN-117 did not show statistically significant differences favorable to the investigational products between the treatment and comparator groups on all the trials' primary, secondary and/or exploratory endpoints. While these studies were not powered for statistical significance, regulatory authorities may find that the studies do not support, in combination with other studies, approval of our product candidates for the target indication. In addition, our product candidates may be associated with undesirable side effects or have characteristics that are unexpected, which may result in abandoning their development or regulatory authorities restricting or denying marketing approval. For instance, prior clinical studies indicated that MIN-101 and MIN-117 may cause adverse events, including, but not limited to, dizziness, vital sign changes, central nervous system events, cardiac events, including prolongation of the QT/QTc interval, and gastrointestinal events. Most product candidates

that commence clinical trials are never approved by the applicable regulatory authorities.

In the case of our product candidates, MIN-101 and MIN-117, we are seeking to develop treatments for schizophrenia and MDD, which adds a layer of complexity to our clinical trials and may delay regulatory approval. We do not fully understand the cause and pathophysiology of schizophrenia and MDD, and our results will rely on subjective subject feedback, which is inherently difficult to evaluate, can be influenced by factors outside of our control and can vary widely from day to day for a particular subject, and from subject to subject and site to site within a clinical study. The placebo effect may also have a more significant impact on our clinical trials.

If our product candidates are not shown to be both safe and effective in clinical trials, we will not be able to obtain regulatory approval or commercialize our product candidates.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and management resources, we focus on a limited number of research programs and product candidates. For instance, at the present time we are prioritizing the clinical trials and development of the most advanced of our product candidates, MIN-101. As a result, we may forego or delay pursuit of opportunities with other product candidates, including MIN-117, MIN-202 and MIN-301, or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights.

Even if we complete the necessary clinical trials, we cannot predict when or if we will obtain marketing approval to commercialize a product candidate or the approval may be for a more narrow indication than we expect.

We cannot commercialize a product candidate until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if our product candidates demonstrate safety and efficacy in clinical trials, the regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain marketing approval from the relevant regulatory agencies. Additional delays may result if the EMA, FDA, an FDA Advisory Committee, or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical trials and the review process.

Even if our product candidates receive regulatory approval, they may still face future development and regulatory difficulties, including ongoing regulatory obligations and continued regulatory review. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to administrative sanctions or penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

Even if we obtain regulatory approval for a product candidate, product candidates may be approved for fewer or more limited indications, including more limited subject populations, than we request, and regulatory authorities may require that contraindications, warnings, or precautions be included in the product labeling, including a black box warning, may grant approval contingent on the performance of costly post-marketing clinical trials or other post-market requirements, such as REMS, may require post-marketing surveillance, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. For instance, in 2007, the FDA requested that makers of all antidepressant medications update existing black box warnings about increased risk of suicidal thought and behavior in young adults, ages 18 to 24, during initial treatment. If approved for marketing, our drugs may be required to carry warnings similar to this and other class-wide warnings.

Any approved products would further be subject to ongoing requirements imposed by the EMA, FDA, and other comparable foreign regulatory authorities governing the manufacture, quality control, further development, labeling, packaging, storage, distribution, safety surveillance, import, export, advertising, promotion, marketing, recordkeeping and reporting of safety and other post-market information. If there are any modifications to the drug, including changes in indications, labeling, manufacturing processes or facilities, or if new safety issues arise, a new or supplemental NDA, post-implementation notification or other reporting may be required or requested, which may

require additional data or additional pre-clinical studies and clinical trials.

The EMA, FDA and other comparable foreign regulatory authorities will continue to closely monitor the safety profile of any product even after approval. If the EMA, FDA or other comparable foreign regulatory authorities become aware of new adverse safety information after approval of any of our product candidates, a number of potentially significant negative consequences could result, including:

- we may suspend marketing of, or withdraw or recall, such product;
- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings or otherwise restrict the product's indicated use, label, or marketing;
- the EMA, FDA or other comparable foreign regulatory bodies may issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings about such product;
- the FDA may require the establishment or modification of a REMS or the EMA or a comparable foreign regulatory authority may require the establishment or modification of a similar strategy that may, for instance, require us to issue a

medication guide outlining the risks of such side effects for distribution to subjects or restrict distribution of our products and impose burdensome implementation requirements on us;
- regulatory authorities may require that we conduct post-marketing studies or surveillance;
- we could be sued and held liable for harm caused to subjects or patients; and
- our reputation may suffer.

In addition, manufacturers of drug products and their facilities, including contracted facilities, are subject to continual review and periodic inspections by national regulatory authorities in the European Union, the FDA and other regulatory authorities for compliance with current Good Manufacturing Practices, or cGMP, regulations and standards. The European Union cGMP guidelines are as set forth in Commission Directive 2003/94/EC of October 8, 2003. If we or a regulatory agency or authority discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, the product's stability (changes in levels of impurities or dissolution profile) or problems with the facility where the product is manufactured, we may be subject to reporting obligations, additional testing and additional sampling, and a regulatory agency or authority may impose restrictions on that product, the manufacturing facility, our suppliers, or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. If we, our product candidates, the manufacturing facilities for our product candidates, our CROs, or other persons or entities working on our behalf fail to comply with applicable regulatory requirements either before or after marketing approval, a regulatory agency may, depending on the stage of product development and approval:

- issue adverse inspectional findings;
- issue Warning Letters, Cyber Letters or Untitled Letters;
- mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners;
    - amend and update labels or package inserts;
- require us to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- seek an injunction or impose civil, criminal and/or administrative penalties, damages or monetary fines or imprisonment;
- suspend or withdraw regulatory approval;
- suspend or terminate any ongoing clinical studies;
- bar us from submitting or assisting in the submission of new regulatory applications;
- refuse to approve pending applications or supplements to applications filed by us;
- refuse to allow us to enter into government contracts;
- suspend or impose restrictions on operations, including restrictions on marketing or manufacturing of the product, or the imposition of costly new manufacturing requirements or use of alternative suppliers; or
- seize or detain products, refuse to permit the import or export of products, or require us to initiate a product recall.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our products and generate revenue.

Our product candidates and the activities associated with their development and commercialization in the United States, including, but not limited to, their advertising and promotion, will further be heavily scrutinized by the FDA, the United States Department of Justice, the United States Department of Health and Human Services' Office of Inspector General, state attorneys general, members of Congress and the public. Violations of applicable law, including advertising, marketing and promotion of our products for unapproved (or off-label) uses, are subject to enforcement letters, inquiries and investigations, and civil, criminal and/or administrative sanctions by regulatory agencies. Additionally, comparable foreign regulatory authorities will heavily scrutinize advertising and promotion of any product candidate that obtains approval outside of the United States. In this regard, advertising and promotion of medicines in the European Union is governed by Directive 2001/83 EC, as amended, and any such activities which we

may undertake in the European Union will have to be in strict compliance with the same. Any advertising of a prescription medicinal product to the public and any promotion of a medicinal product that does not have marketing authorization or is not promoted in accordance with that marketing authorization is prohibited. Advertisements and promotions of medicinal products are monitored nationally in the European Union, and each country will have its own additional advertising laws and industry governing bodies, whose obligations may go further than those set out in Directive 2001/83. For instance, in the United Kingdom the code of practice of the Association of the British Pharmaceutical Industry (the lead United Kingdom trade association) is considerably stricter than applicable legislative requirements. Any violations and sanctions will similarly be decided and administered by the relevant country's national authority.

In the United States, engaging in the impermissible promotion of products for off-label uses can also subject the entity engaging in such conduct to false claims litigation under federal and state statutes, which can lead to civil, criminal and/or administrative penalties, damages, monetary fines, disgorgement, exclusion from participation in Medicare, Medicaid and other federal healthcare programs, curtailment or restructuring of its operations and agreements that materially restrict the manner in which it promotes or distributes drug products. Accordingly, we are subject to the federal civil False Claims Act, which prohibits persons and entities from knowingly filing, or causing to be filed, a false claim, or the knowing use of false statements, to obtain payment from the federal government. Certain suits filed under the civil False Claims Act, known as "qui tam" actions, can be brought by any individual on behalf of the government and such individuals, commonly known as "whistleblowers," may share in certain amounts paid by the entity to the government in fines or settlement. When an entity is determined to have violated the civil False Claims Act, it may be required to pay

up to three times the actual damages sustained by the government, plus civil penalties for each separate false claim. Various states have also enacted laws modeled after the federal civil False Claims Act. We are also subject to the federal criminal False Claims Act, which imposes criminal fines or imprisonment against individuals or entities who make or present a claim to the government knowing such claim to be false, fictitious, or fraudulent. Additionally, we may be subject to civil monetary penalties that may be imposed against any person or entity that, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

False Claims Act lawsuits against pharmaceutical companies have increased significantly in volume and breadth, leading to substantial civil and criminal settlements regarding certain sales practices, including promoting off-label drug uses. This growth in litigation has increased the risk that a pharmaceutical company will have to defend a false claims action, pay settlement fines or restitution, agree to comply with burdensome reporting and compliance obligations, and/or be excluded from Medicare, Medicaid and other federal and state healthcare programs. If we do not lawfully promote our products, we may become subject to such litigation, which may have a material adverse effect on our business, financial condition and results of operations.

While no definition of “off-label use” exists at the European Union level, promotion of a medicinal product for a purpose that has not been approved is strictly prohibited. Such promotion also gives rise to criminal prosecution in the European Union, and national healthcare supervisory authorities may impose administrative fines. Engaging in such promotions in the European Union could also lead to product liability claims, in accordance with EU product liability regime under Directive 85/374.

The EMA’s, FDA’s, and other applicable government agencies’ policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval and marketing authorization, and the sale and promotion of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and be subject to civil, criminal and administrative enforcement, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

The regulatory pathway for our product candidate, MIN-301, has not yet been determined. Depending on the pathway, we may be subject to different regulatory requirements.

MIN-301 is a peptide, and, as a peptide, may be subject to the Public Health Service Act, or PHSA, and the Food, Drug, and Cosmetic Act, or FDCA. We have yet to meet with the FDA regarding the approval pathway for this product candidate. Based on the definition of a biologic in the PHSA, we believe that MIN-301 meets the definition of a biologic and, thus, we will need to submit a Biologics License Application, or BLA, for product approval. Moreover, based on an FDA intercenter agreement, we believe that MIN-301 will be regulated by the FDA’s Center for Drug Evaluation and Research. However, we intend to discuss jurisdiction with the FDA to determine the appropriate regulatory pathway and corresponding requirements. Depending on the pathway, we may be subject to different regulatory requirements, including different regulatory and testing requirements, shorter or longer periods of market exclusivity, and different approval processes for generic drug and biosimilar competitors.

If the market opportunities for any product that we or our collaborators develop are smaller than we believe, our revenue may be adversely affected and our business may suffer.

Our product candidates are intended for the treatment of schizophrenia, MDD, insomnia and Parkinson’s disease. Our projections of both the number of people who have these disorders or disease, as well as the subsets of people who have the potential to benefit from treatment with our product candidates and who will pursue such treatment, are based on our beliefs and estimates that may prove to be inaccurate. For instance, with respect to schizophrenia and MDD,

our estimates are based on the number of patients that suffer from schizophrenia and MDD, but these disorders are difficult to accurately diagnose and high rates of patients may not seek or continue treatment. Our estimates and beliefs are also based on the potential market of other drugs in development for schizophrenia and MDD, which may prove to be inaccurate and our advantages over such drugs may not be, or may not be perceived to be, as significant as we believe they are. If our estimates prove to be inaccurate, even if our products are approved, we may not be able to successfully commercialize them. In addition, the cause and pathophysiology of schizophrenia and MDD are not fully understood, and additional scientific understanding and future drug or non-drug therapies may make our product candidates obsolete.

Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates are developed through pre-clinical to late stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or future clinical trials to be conducted with the altered materials. Such changes may also require additional testing, EMA or FDA notification or EMA or FDA

approval. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and/or jeopardize our ability to commence product sales and generate revenue.

Our failure to obtain regulatory approval in additional international jurisdictions would prevent us from marketing our product candidates outside the European Union and the United States.

We plan to seek regulatory approval to commercialize our product candidates in the European Union and, other than MIN-202, in the United States. We also expect to seek regulatory approval in additional foreign countries. To market and sell our products in other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain EMA or FDA approval. The regulatory approval process outside the European Union and United States generally includes risks substantially similar to those associated with obtaining EMA or FDA approval. In addition, in many countries outside the United States, we must secure product price and reimbursement approvals before regulatory authorities will approve the product for sale in that country or within a short time after receiving such marketing approval. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries and regulatory approval in one country does not ensure approval in any other country, while a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. Also, regulatory approval for any of our product candidates may be withdrawn. If we fail to comply with the regulatory requirements in international markets or do not receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed and our business will be adversely affected. We may not obtain foreign regulatory approvals on a timely basis, if at all, especially because some foreign jurisdictions require prior approval of a treatment by the domestic regulatory agency. Our failure to obtain approval of any of our product candidates by regulatory authorities in another country may significantly diminish the commercial prospects of that product candidate and our business prospects could decline.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than us.

The biopharmaceutical industry is intensely competitive and subject to rapid and significant technological change. We face competition with respect to our current product candidates and will face competition with respect to any future product candidates from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. Many of our competitors have significantly greater financial, technical and human resources. Smaller and early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

Our competitors may obtain regulatory approval of their products more rapidly than us or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product candidates. Our competitors may also develop drugs that are more effective, more convenient, more widely used, less costly and/or have a better safety profile than our products, and competitors may also be more successful than us in manufacturing and marketing their products.

Our competitors will also compete with us in recruiting and retaining qualified scientific, management and commercial personnel, establishing clinical trial sites and subject registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

There are numerous currently approved therapies for treating the same diseases or indications for which our product candidates may be useful and many of these currently approved therapies act through mechanisms similar to our product candidates. Many of these approved drugs are well-established therapies or products and are widely accepted by physicians, patients and third-party payors. Some of these drugs are branded and subject to patent protection and regulatory exclusivity, while others are available on a generic basis. Insurers and other third-party payors may encourage the use of generic products or specific branded products. Moreover, it is difficult to predict the effect that introduction of biosimilars into the market will have on sales of the reference biologic product, which will depend on the FDA's standards for interchangeability, the structure of government and commercial managed care formularies, and state laws on substitution of biosimilars. We expect that if our product candidates are approved, they will be priced at a significant premium over competitive generics and biosimilars. This may make it difficult for us to differentiate our products from currently approved therapies, which may adversely impact our business strategy. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability, and safety in order to overcome price competition and to be commercially successful. If we are not able to compete effectively against our current and future competitors, our business will not grow and our financial condition and operations will suffer. Moreover, many companies are developing new therapeutics, and we cannot predict what the standard of care will be as our product candidates progress through clinical development.

Even if any of our drug candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If any of our drug candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success. If our drug candidates do not achieve an adequate level of acceptance, we may not generate significant revenue from drug sales and we may not become profitable. Our commercial success also depends on coverage and adequate reimbursement of our products by third-party payors, including government payors, which may be difficult or time-consuming to obtain, may be limited in scope or may not be obtained in all jurisdictions in which we may seek to market our products. The degree of market acceptance of our drug candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and perceived and potential advantages compared to alternative treatments, including any similar generics and biosimilars;
- the timing of market introduction relative to alternative treatment;
- our ability to offer our drugs for sale at competitive prices relative to alternative treatments;
- the clinical indications for which the product candidate is approved;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of our marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement for our products or the willingness of patients to pay out-of-pocket in the absence of coverage and adequate reimbursement by third-party payors;
- unfavorable publicity relating to the products;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our drugs together with other medications.

Our focus on CNS disorders, in particular, exposes us to an increased risk that serious side effects and disease events, including suicide, will occur during patient use of our products, even if such side effects and disease events are unrelated to the use of our products. Most approved CNS medicines carry boxed warnings for clinically significant adverse events, and our products may categorically need to carry such warnings as well.

We currently have no marketing and sales organization. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, we may not be able to effectively market and sell our product candidates, if approved, or generate product revenues.

We currently do not have a marketing or sales organization for the marketing, sales and distribution of pharmaceutical products. In order to commercialize any product candidates, we must build our marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so on commercially reasonable terms or at all.

If our product candidates receive regulatory approval, we intend to establish our sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize our product candidates, which will be expensive and time consuming and may require substantial investments prior to any product candidate being granted regulatory approval. In selling, marketing and distributing our products ourselves, we face a number of additional risks, including:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or educate adequate numbers of physicians on the clinical benefits of our products to achieve market acceptance;

- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- the costs associated with training sales personnel on legal compliance matters and monitoring their actions;
- liability for sales personnel failing to comply with the applicable legal requirements; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products.

We may choose to collaborate with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. If we enter into arrangements with third parties to perform sales, marketing and distribution services for our products, the resulting revenues or the profitability from these revenues to us are likely to be lower than if we had sold, marketed and distributed our products ourselves. If we are unable to enter into such arrangements on acceptable terms or at all, we may not be able to successfully commercialize any of our product candidates that receive regulatory approval. Depending on the nature of the third party relationship, we may have little control over such third parties, and any of these third parties may fail to devote the necessary resources and attention to sell, market and distribute our products effectively.

If we are not successful in commercializing our product candidates, either on our own or through collaborations with one or more third parties, our future product revenue will suffer and we may incur significant additional losses.

Even if we commercialize any of our product candidates, these products may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which could harm our business.

The laws that govern marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. In many countries, the pricing review period begins after marketing or product licensing approval is granted. Some countries require approval of the sale price of a drug before it can be marketed or soon thereafter. Additionally, in some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, which could negatively impact the revenues we generate from the sale of the product in that particular country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates even if our product candidates obtain marketing approval.

In the European Union, the pricing and reimbursement of prescription drugs is controlled by each member state. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures in the current economic climate in Europe. There is very limited harmonization on member state pricing and reimbursement practices in the European Union.

Reference pricing used by various European Union member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In particular, Germany, Portugal and Spain have all introduced a number of short-term measures to lower healthcare spending, including mandatory discounts, clawbacks and price referencing rules, which could have a material adverse effect on our business.

Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, determine which medications they will cover and establish reimbursement levels. Assuming we obtain coverage for a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover all or a significant portion of the cost of our products. Therefore, coverage and adequate reimbursement is critical to new

product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available.

Government authorities and other third-party payors are developing increasingly sophisticated methods of controlling healthcare costs, such as by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices as a condition of coverage, are using restrictive formularies and preferred drug lists to leverage greater discounts in competitive classes, and are challenging the prices charged for medical products. In addition, in the United States, federal programs impose penalties on drug manufacturers in the form of mandatory additional rebates and/or discounts if commercial prices increase at a rate greater than the Consumer Price Index-Urban, and these rebates and/or discounts, which can be substantial, may impact our ability to raise commercial prices. Further, no uniform policy requirement for coverage and reimbursement for drug products exists among third-party payors in the United States. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.