Minerva Neurosciences, Inc.
Form 10-K
March 12, 2018

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2017

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 286 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

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

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405) 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, a smaller reporting company, or an emerging growth company. See the definition of "large accelerated filer", "accelerated filer", "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer		Accelerated filer
Non-accelerated filer	(Do not check if a smaller reporting company)	Smaller reporting company
Emerging growth company		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

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

The aggregate value of the Company's Common Stock held by non-affiliates of the Company was approximately $238.6 million as of June 30, 2017, the last day of the Company's most recently completed second fiscal quarter, when the last reported sales price was $8.85 per share.

The number of shares of Registrant's Common Stock outstanding as of March 9, 2018 was 38,749,343.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Definitive Proxy Statement relating to the 2018 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, 2017.

MINERVA NEUROSCIENCES, INC.

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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 may potentially address the unmet needs of patients with these diseases.

Our product portfolio and potential indications include: roluperidone (also known as MIN-101) for the treatment of schizophrenia; seltorexant (also known as MIN-202 or JNJ-42847922), which we are co-developing with Janssen Pharmaceutica NV, or Janssen, for the treatment of insomnia disorder and 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 2017 approximately 2.8 million people suffered from schizophrenia, 29.0 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 as a symptom affects up to 50% of the general population, while insomnia with significant daytime consequences is estimated to affect 7% to 13% of the population worldwide and is recognized as a major public health issue.

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 differentiated products with novel mechanisms of action that target therapeutic areas of high unmet need and significant disease burden; attention to patient safety and compliance; scientific rigor applied to patient selection and clinical trial conduct; engagement of highly trained clinical trial investigators; incorporation of patient and caregiver insights to drive clinical advancements; and integrity. With the experience and knowledge base of our clinicians and physicians, we have generated substantive data from randomized, double blind, placebo-controlled trials that support the clinical advancement of these products in defined patient populations and in several regulatory jurisdictions. In summary, key elements of our strategy are:

- Identify, acquire and develop differentiated products with innovative mechanisms of action based on biological and clinical insights into the unmet needs of patients;
- Leverage the randomized, double-blind, placebo-controlled data from completed proof-of-principle trials to advance the clinical development of our product candidates in multiple regulatory jurisdictions;

- Prepare for the commercialization of our lead product, roluperidone, based on its differentiated profile as a potential monotherapy in schizophrenia and, in the longer term as a potential treatment for other degenerative brain disorders in which negative symptoms represent a significant debilitating, unmet need;
- Selectively explore collaborations with leading pharmaceutical companies to maximize the value of our current product candidate portfolio, particularly in connection with pivotal 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 to investigate with 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 roluperidone 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 roluperidone 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 Sarl, or Mind-NRG, which had exclusive rights to develop and commercialize MIN-301 globally. 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, subsequently amended in June 2017, we are co-developing seltorexant 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.

We have not received regulatory approvals to commercialize any of our product candidates, and we have not generated any revenue from the sales or license of our product candidates. We have incurred significant operating losses since inception. We expect to incur net losses and negative cash flow from operating activities for the foreseeable future in connection with the clinical development and the potential regulatory approval, infrastructure development and commercialization of our product candidates.

Our Pipeline

Roluperidone (MIN-101)

Introduction

Roluperidone 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 roluperidone to treat patients with schizophrenia. Roluperidone has been designed 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. Roluperidone has also been designed to block a specific subtype of sigma receptor called sigma-2, which is involved in movement control, psychotic symptom control and learning and memory. Blocking sigma-2 also increases calcium levels in neurons in the brain, which can improve memory.

We believe the scientifically supported and innovative mechanisms of action of roluperidone may potentially address the unmet needs of schizophrenic patients, which include negative symptoms and cognitive impairment, as well as the side effects of existing therapies. We plan to seek approval of roluperidone initially as a first line monotherapy to treat negative symptoms in patients diagnosed with schizophrenia, and we also may study its use in monotherapy or in combination with approved atypical antipsychotic agents to treat all aspects of the disease, including positive symptoms and relapse prevention. We believe that roluperidone, if approved, could treat the majority of patients diagnosed with schizophrenia. An estimated 69% of patients diagnosed with schizophrenia have negative symptoms, with at least 42% of patients diagnosed with schizophrenia having prominent negative symptoms. Beyond schizophrenia,

we believe roluperidone may possess therapeutic utility in degenerative brain disorders where negative symptoms constitute a significant unmet need.

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

Clinical Development

Phase 3 Clinical Trial

On December 19, 2017, we announced the screening of the first patient in the pivotal Phase 3 clinical trial of roluperidone (Study MIN-101C07) as monotherapy for negative symptoms in patients diagnosed with schizophrenia. The trial is a multicenter, randomized, double-blind, parallel-group, placebo-controlled, 12-week study to evaluate the efficacy and safety of 32 milligrams, or mg, and 64 mg of roluperidone in adult patients with negative symptoms of schizophrenia. The 12-week study will be followed by a 40-week, open-label extension period during which patients on drug will continue receiving their original dose and patients on placebo will receive either 32 mg or 64 mg of roluperidone.

Approximately 500 patients will be enrolled in this trial at approximately 60 clinical sites in the U.S. and Europe, with about 30 percent of patients coming from the U.S. Patients will be initially randomized equally to receive one of the two doses of roluperidone or placebo for 12 weeks. Thereafter, all patients will continue treatment with active drug for the 40-week extension period. Top-line results from the 12-week double blind phase of this trial are expected in the first half of 2019.

The primary endpoint of this trial will be improvement in negative symptoms in patients treated with roluperidone compared to placebo as measured by the change in the Positive and Negative Syndrome Scale, or PANSS, Marder negative symptoms factor score, or NSFS, over the 12-week double-blind treatment period. To support the use of the Marder NSFS as the primary endpoint in the Phase 3 study, it was applied to the Phase 2b PANSS data, and the resulting analysis confirmed the robustness of the effect of roluperidone for the two tested doses. The key secondary endpoint will be the effect of roluperidone compared to placebo as measured by the Personal and Social Performance, or PSP, total score over the same period. Additional secondary endpoints will be the effect of roluperidone compared to placebo on the Clinical Global Impression of Severity, or CGI-S, score and safety and tolerability.

Patients admitted into the trial must have a documented diagnosis of schizophrenia for at least one year and be symptomatically stable for at least 6 months with moderate to severe negative symptoms (>20 on the PANSS negative symptom subscale) and stable positive symptoms. Patients without severe symptoms of excitement/hyperactivity, suspiciousness, persecution, hostility, uncooperativeness, or poor impulse control will be recruited. We believe these eligibility criteria represent the real-world patient population who may benefit when the drug is used in clinical practice. In addition, patients treated with psychotropic agents will need to undergo wash-out before receiving study drug. These parameters were applied in screening the population treated in the Phase 2b trial.

Chemistry, Manufacturing and Controls (CMC) program

The CMC scale-up program for roluperidone is ongoing to ensure consistency between the drug batches to be used during pivotal, Phase 3 testing and those that will be available for potential marketing and commercialization pending the completion of our Phase 3 trial and subsequent regulatory submission and review of a New Drug Application (NDA) for roluperidone. The CMC program requires validation of all aspects of the manufacturing processes required to result in a drug product that consistently meets approved quality standards.

Improved Formulation

On June 22, 2017, we announced the completion of a bridging trial to select an improved, gastro-resistant, or GR, formulation of roluperidone that we are using in the Phase 3 clinical trial with roluperidone and to include in the potential future submission of an NDA.

Data from the bridging trial of the selected new formulation demonstrated the following: single oral dose administration of the GR formulation in study MIN-101C06, C_{max} was approximately 70% and 80% of those seen with the MR32 formulation administration for roluperidone and BFB-520 (a metabolite of roluperidone), respectively; no reduction in the extent of exposure (AUC_{inf}) for the GR formulation as compared to the formulation used in the Phase 2b study (MR formulation) with a relative bioavailability of 101% and 96.1%, and a delayed T_{max} from 2.4 hours to 6.0 hours and from 6.9 hours to 12.5 hours for roluperidone and BFB-520, respectively; no food effect was observed with this formulation with ratios fed vs fasted of 1.04 and 0.96, respectively. These observed reductions in C_{max} are expected to reduce the potential for transient QTc increases observed in the Phase 2b study at the higher dose, 64 mg, but not the lower dose, 32 mg; no observations of QTc prolongations throughout the bridging trial; no observable

food effect, thus allowing administration of the drug with or without food without changing its pharmacokinetic properties; and confirmation of the overall safety and tolerability profile of roluperidone.

As exposures of roluperidone in the Phase 2b study and the GR formulation to be used in the Phase 3 trial are comparable, and as the two tested doses are the same for both the Phase 2b and 3 studies, we believe data from both of these studies could collectively form the basis of evaluating efficacy. We have also filed a patent application for the GR formulation, which is in addition to an already granted patent in the U.S. that provides protection until 2035. If granted, the additional patent could potentially extend exclusivity beyond 2035.

End-of-Phase 2 Meeting

In May 2017, we announced the outcome of an “end-of-Phase 2” meeting with the FDA and announced our plans to initiate Phase 3 development of roluperidone. This meeting and additional discussions with the FDA on the Phase 3 trial design and operational conduct led to the finalization of the protocol and design for that trial described above.

Phase 2b Trial

In May 2016, we announced top line results from a prospective Phase 2b, 12-week, randomized, double-blind, placebo-controlled parallel clinical trial evaluating the efficacy, safety and tolerability of roluperidone as monotherapy in patients with negative symptoms of schizophrenia using the pentagonal structure model, or PSM, of PANSS. These negative symptoms, for which no approved treatment is currently available, affect the majority of schizophrenic patients and can persist over their lifetimes. A total of 244 patients were randomized in equal groups to receive daily doses of roluperidone 32 mg, roluperidone 64 mg or placebo at 32 clinical sites in Russia and five European countries. To participate in the trial, patients were required to have stable positive and negative symptoms for three months prior to entering the study, a PANSS negative sub-score greater than or equal to 20, and scores < 4 on the following PANSS items: excitement/hyperactivity, suspiciousness, persecution, hostility, uncooperativeness, or poor impulse control. All three cohorts were balanced with respect to demographic and baseline disease characteristics.

The study met its primary endpoint, as we observed a statistically significant benefit of roluperidone over placebo in improving negative symptoms as measured by the PSM of PANSS. The effect was observed for both doses tested: 32 mg: $p \leq 0.024$ with an effect size of 0.45, and 64 mg: $p \leq 0.004$ with effect size of 0.57.

We also observed a statistically significant benefit of roluperidone over placebo on the PANSS negative symptoms subscale for both doses tested: 32 mg: $p \leq 0.006$, with an effect size of 0.54, and 64 mg: $p \leq 0.001$ with an effect size of 0.70.

Furthermore, we observed the statistically significant benefit of roluperidone over placebo on the PANSS total score (not significant for the 32 mg dose; $p \leq 0.003$ for the 64 mg dose), with effect sizes of 0.34 and 0.57, respectively.

The consistency and robustness of the effect was also supported by the observed statistically significant benefit of roluperidone over placebo in multiple other secondary endpoints as measured by the following: the PANSS general psychopathology subscale, Brief Negative Symptoms Scale total score, Clinical Global Impression of Severity, Clinical Global Impression of Improvement, Personal and Social Performance and Brief Assessment of Cognition in Schizophrenia (BACS). Positive symptoms were observed to remain stable, and the absence of extra-pyramidal symptoms (EPS) throughout the three month trial is consistent with the hypothesis that roluperidone has a direct and specific effect on negative symptoms rather than an indirect effect mediated by improvements of positive symptoms.

Discontinuation criteria based on QTcF prolongation were incorporated in the protocol. Two patients out of 162 who received roluperidone were discontinued based upon these criteria; both of these patients received the higher dose (64

mg).

Patients who completed the 12-week double-blind core phase of this study were provided the opportunity to enter into a 24-week, open-label extension phase. The extension phase was completed during the third quarter of 2016, and we announced data from the extension phase in October 2016. Data generated during the extension period were intended to provide long-term supportive evidence of safety and efficacy and to complement the statistically significant results obtained during the core phase.

During the extension phase, all patients received either 32 mg or 64 mg of roluperidone. Patients who received placebo in the core phase were randomized to one of these two doses at the beginning of the extension phase. One hundred forty-two patients from the treatment and placebo groups in the core phase entered the extension phase, with 88 patients completing the extension. Seventy patients received 32 mg and 72 patients received 64 mg during the extension.

Negative symptoms were observed to continue to improve during the extension phase, as shown by a reduction from the study start for the 32 and 64 mg-treated groups of 5.5 points and 4.9 points, respectively.

Positive symptoms were observed to remain stable throughout the study, as measured by PANSS positive symptom scores. The absence of modification of positive symptoms and the favorable safety and tolerability profile are consistent with the hypothesis that roluperidone has a direct and specific effect on negative symptoms. General psychopathology was observed to improve during the extension phase for the 32 and 64 mg groups, as shown by reductions in the PANSS general psychopathology subscale score.

Roluperidone was generally reported to be well tolerated through the entire 24-week extension phase and no patient was discontinued for QTc increases. In the extension phase, we also observed that roluperidone at the doses tested did not have an effect on EPS, prolactin or weight gain and thus confirmed over a longer period of treatment that we did not observe those common side effects.

Additional data analyses from the Phase 2b trial were presented at the 55th Annual Meeting of the American College of Neuropsychopharmacology, or ACNP in December 2016. These analyses concluded that roluperidone has a direct effect on negative symptoms (rather than an indirect or pseudo effect secondary to improvements in other symptoms) as supported by the stability observed in positive symptoms, the absence of EPS and the persistence of this direct effect even after controlling for improvements in depressive symptoms. Researchers noted that since phenomena similar to negative symptoms are manifest in many neuro-psychiatric disorders and in brain degenerative disorders such as Alzheimer's disease and Parkinson's disease, future trials with roluperidone could be designed to explore its potential benefit in these patient populations.

In post-hoc analysis presented at ACNP, improvement in negative symptoms was shown to be greatest among younger patients. This finding supports the potential therapeutic benefit of roluperidone in patients with schizophrenia who are beginning to manifest these symptoms. It is also consistent with research showing that chronic pharmacotherapeutic intervention in schizophrenia, which includes atypical antipsychotics to treat acute positive symptoms, becomes less effective as patients age and suffer long-term consequences of the disease and side effects of current treatment options, particularly the blockade of dopamine neurotransmitter pathways in the brain.

Additional results presented at ACNP suggest a benefit of treatment with roluperidone in improving cognitive function in schizophrenia patients with predominant negative symptoms. Cognitive function was evaluated using the BACS scale. Cognitive impairment, a core feature of schizophrenia, affects up to 75% of patients and is believed to be a good predictor of functional outcome.

In July 2017, we announced that the American Journal of Psychiatry published online results from the Phase 2b clinical trial of roluperidone in a manuscript, entitled "Efficacy and Safety of MIN-101: A 12-Week Randomized, Double-Blind, Placebo-Controlled Trial of New Drug in Development for the Treatment of Negative Symptoms in Schizophrenia". The key finding from the publication is that roluperidone achieved its primary outcome in the trial, demonstrating statistically significant superiority over placebo in improving negative symptoms in schizophrenia patients. Supporting these findings were similar and concomitant improvements on several secondary outcome measures, including PANSS cluster analyses of negative symptoms, the PANSS total score, the Clinical Global Impression (CGI) and the Brief Negative Symptom Scale (BNSS). Psychosis measured by the PANSS Positive symptoms subscale remained stable during the trial, suggesting that the improvement in negative symptoms associated with roluperidone was specific and not a pseudo-effect secondary to improvements in psychosis.

A second analysis of the Phase 2b data was published in the journal Schizophrenia Research, in the article entitled "The brief negative symptom scale (BNSS): Sensitivity to treatment effects." Researchers concluded that patients treated with 64 mg of MIN-101 showed a significant decrease in BNSS total score, a secondary outcome measure in the

Phase 2b 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 of interest or pleasure in activities, changes in sleep such as insomnia, fatigue and diminished ability to concentrate 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 may 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.

Clinical Development

Phase 2b Trial

Building upon the results of the previous Phase 2a trial with MIN-117 in Europe, we are planning to initiate a Phase 2b trial in MDD in the U.S. and Europe in early 2018. We expect to enroll patients with MDD who also have symptoms of anxiety. In preparation for this trial, a food effect study was recently completed, and the preliminary data show that food has no effect on the exposure PK parameters, therefore allowing dosing with or without food.

Phase 2a Trial

In May 2016, we announced top line results from a Phase 2a clinical trial in MDD with MIN-117. Data from this trial were subsequently presented at the ACNP Annual Meeting in December 2016. This study was a four-arm, parallel-group, randomized double-blind, placebo- and positive-control trial which tested two daily administered doses of MIN-117: 0.5 mg and 2.5 mg. The study included 84 patients (21 per arm) with moderate to severe MDD in four European countries. The goals of the trial were to test efficacy, safety and tolerability of MIN-117 over six weeks of treatment. The antidepressant paroxetine was used as an active control and confirmed assay sensitivity. Change on the Montgomery-Asberg Depression Rating Scale, or MADRS, was used as the main outcome measurement. As established prospectively in the statistical analysis plan, this trial was designed for signal detection and effect size estimation. As such, the study was not powered to demonstrate statistically significant differences between MIN-117 and placebo.

We observed the dose-dependent benefit of MIN-117 over placebo as measured by change in MADRS total scores. We observed that MIN-117 at the 0.5 mg daily dose had an effect size, as compared to the placebo group, of 0.24 while the 2.5 mg daily dose had an effect size of 0.34. This magnitude of effect size is similar to those observed with currently marketed antidepressants. Improvement in MADRS with MIN-117 against placebo was observed at two weeks. Furthermore, data also showed that 24% of the patients treated with 2.5 mg of MIN-117 achieved remission as prospectively defined.

Both doses of MIN-117 were reported to be well tolerated, and the incidence and types of side effects did not differ significantly between the MIN-117 group and the placebo group. No unexpected adverse events were reported. Treatment with MIN-117 was not associated with cognitive impairment, sexual dysfunction, suicidal ideation or weight gain.

Pharmacodynamic measurements based on sleep recordings showed that MIN-117 preserved sleep continuity and architecture and therefore is not expected to have detrimental effects on rapid eye movement sleep distribution and duration.

Seltorexant (MIN-202)

Introduction

Seltorexant is an innovative selective orexin 2 receptor antagonist we are co-developing with Janssen for the treatment of insomnia and as adjunctive therapy for MDD. 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.

In the brain, the orexin system is involved in the control of several key functions, including metabolism and wakefulness. Seltorexant 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. Janssen completed a Phase I single ascending dose study of seltorexant in 2011 that suggested a relationship which supports a rapid induction and promotion of sleepiness.

We are co-developing seltorexant with Janssen and own the exclusive rights to develop and commercialize the compound in the Minerva Territory subject to royalty payments to Janssen and we have the right to receive royalties on any sales outside the Minerva Territory.

Amendment to Co-Development and License Agreement with Janssen

In June 2017, we entered into an agreement with Janssen to amend our Co-Development and License Agreement for seltorexant. The effectiveness of this amendment, or the Amendment, was contingent upon approval of its terms by the European Commission and the closing of the acquisition of Actelion by affiliates of Janssen. These conditions were subsequently met, and the agreement became effective on August 29, 2017.

Under the amended agreement, Janssen has waived its right to royalties on seltorexant insomnia sales in the European Union, Switzerland, Liechtenstein, Iceland and Norway, or the Minerva Territory. We retain all of our rights to seltorexant, including commercialization of the molecule for the treatment of insomnia and as an adjunctive therapy for MDD, which include an exclusive license in the Minerva Territory, with royalties payable by us to Janssen. Royalties on sales outside of the Minerva Territory are payable by Janssen to us. Janssen made an upfront payment to us of $30 million upon the effectiveness of the Amendment and agreed to make a $20 million payment at the start of a Phase 3 insomnia trial for seltorexant and a $20 million payment when 50% of the patients are enrolled in this trial. Janssen further agreed to waive the remaining payments due from us until completion of the Phase 2 development of seltorexant. The $30 million payment and $11.2 million in previously accrued collaborative expenses, which were forgiven upon the effective date of the agreement, will be earned and recognized as revenue as the services are performed from the commencement of Phase 3 development to the completion of the development activities using the proportional performance method. The $30 million payment along with the $11.2 million previously accrued collaborative expenses have been included under deferred revenue on our balance sheet at December 31, 2017.

As a result of the Amendment, we assumed strategic control for the clinical development of seltorexant in insomnia under the Phase 2 development program, but we have no further financial obligations until the Phase 2b development milestone is complete, which is expected to occur in the second half of 2019. Upon completion of this development milestone, referred to as “Decision Point 4”, we have the right to opt-out of the agreement and collect a royalty on worldwide sales of seltorexant in the single digits with no further obligations to Janssen. If we elect to continue to Phase 3, we would be obligated to fund the clinical trials related to insomnia, and receive $40 million in milestone payments from Janssen, and would also be responsible for 40% of the development costs in the Phase 3 MDD program. In connection with the Amendment, we also repurchased all of the approximately 3.9 million shares of our stock previously owned by Johnson & Johnson Innovation-JJDC Inc. at a per share price of $0.0001, for an aggregate purchase price of approximately $389.

Clinical Development

Phase 2b Trials in MDD

On September 5, 2017, we announced the enrollment of the first patient in a Phase 2b trial of seltorexant as adjunctive therapy to antidepressants in adult patients with MDD who have responded inadequately to antidepressant therapy. The primary objectives of this multi-center, double-blind, randomized, parallel group, placebo-controlled, adaptive-dose finding study are to assess the dose-response relationship and augmentation of antidepressant effects of up to three doses of seltorexant (10 mg, 20 mg and 40mg) and to assess the safety and tolerability of seltorexant compared to placebo. The trial consists of three phases: a screening phase lasting up to four weeks, a six-week double-blind treatment phase and a two-week post-treatment follow-up phase. We plan to enroll approximately 280 patients at approximately 85 clinical sites in the U.S., Europe, Russia and Japan.

On December 21, 2017, we announced the enrollment of the first patient in a Phase 2b clinical trial comparing seltorexant versus quetiapine as adjunctive therapy in patients with MDD who have responded inadequately to antidepressant therapy. The primary objective of this multi-center, double-blind, randomized, flexible-dose, parallel-group study is to assess the efficacy of flexibly dosed seltorexant compared to flexibly dosed quetiapine as adjunctive therapy to a baseline antidepressant drug in delaying time to all-cause discontinuation of study drug over a 6-month treatment period. Time to all-cause discontinuation is defined as the number of days from administration of the first dose of study drug to administration of the last dose of study drug.

The trial consists of three phases: a screening phase lasting up to four weeks, a six-month double-blind treatment phase and a two-week follow-up phase. Approximately 100 patients 18 to 64 years of age are planned to be randomized at approximately 34 sites in the U.S. to receive either flexibly dosed seltorexant, 20 mg or 40 mg, or flexibly dosed quetiapine XR, 150 mg or 300 mg. Subjects will continue to take their baseline antidepressant therapy of either an SSRI (selective serotonin reuptake inhibitor) or an SNRI (serotonin-norepinephrine reuptake inhibitor) at the same dose throughout the screening, double-blind and follow-up phases.

Phase 2b Trial in Insomnia Disorder

On December 6, 2017, we announced the enrollment of the first patient in a Phase 2b clinical trial of seltorexant in patients with insomnia disorder. This multicenter, double-blind, randomized, parallel-group, active- and placebo-controlled dose finding study is designed to assess the efficacy and safety of seltorexant in both adult and elderly subjects with insomnia disorder. The primary objective of this trial is to assess the dose-response of three doses of seltorexant (5, 10 and 20 mg daily) compared to placebo on sleep onset as measured by the latency to persistent sleep (LPS) using polysomnography (PSG). The key secondary objective is to assess the dose-response of these three doses compared to placebo on wake after sleep onset (WASO) over the first six hours using PSG. In addition, the effects of seltorexant on sleep and cognition will be compared to those effects of zolpidem to determine potential differences between the compounds.

A total of approximately 360 patients 18 to 85 years of age will be randomized in this study at clinical sites in the United States, European Union and Japan. The duration of participation in this study for an individual subject will be up to 61 days, including screening and follow-up.

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 and potentially for other neurodegenerative disorders. 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 is a peptide that contains the extracellular domain of the human neureglin-1 beta 1 protein and is produced using an Escherichia coli organism that is genetically engineered to express this 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.

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.

We previously 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. We believe these data provide support for advancing MIN-301 into clinical trials for the treatment of Parkinson's disease in humans. Building upon these data, we are continuing to conduct preclinical studies in preparation for an IND or Investigational Medicinal Product Dossier, or IMPD, filing, with a Phase 1 study expected to commence thereafter.

License Agreements

Roluperidone License Agreement with MTPC

We have entered into a license agreement with MTPC dated as of August 30, 2007, as amended, or the Roluperidone License Agreement. Under the terms of the Roluperidone License Agreement, we acquired an exclusive license to the lead compound known as CYR-101 (subsequently renamed roluperidone), 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 Roluperidone 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 Roluperidone 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 roluperidone and up to $59.5 million for additional products.

In January 2014, we renegotiated the structure of the license for roluperidone 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, as well as the tiered royalty payments described above. 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 roluperidone 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, we 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, we paid MTPC, and recorded an expense for, $80,000 in the year ended December 31, 2015. We met the enrollment milestone obligation in June 2015.

Seltorexant Co-Development and License Agreement with Janssen

On February 13, 2014, we signed a co-development and license agreement (“the agreement”) with Janssen, which became effective upon completion of our initial public offering and the payment of a $22.0 million license fee. Under the agreement, Janssen, the licensor, granted us an exclusive license, with the right to sublicense, in the Minerva Territory, under (i) certain patent and patent applications to sell products containing any orexin 2 compound, controlled by the licensor and claimed in a licensor patent right as an active ingredient and (ii) seltorexant 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 seltorexant, also known as JNJ-42847922. We have granted to the licensor an exclusive license, with the right to sublicense, under all patent rights and know-how controlled by us related to seltorexant to sell seltorexant outside the Minerva Territory. In consideration of the licenses granted on July 7, 2014, we made a license fee payment of $22.0 million, which was included as a component of research and development expense in 2014.

The original agreement contains certain provisions, which include our ability to opt-out of the agreement upon completion of certain milestones. If we elect to participate in the development program through to the potential commercial approval of seltorexant we will pay a quarterly royalty percentage to the licensor in the high single digits on aggregate net sales for seltorexant products sold by us, our affiliates and sublicensees in the Minerva Territory. The licensor will pay a quarterly royalty percentage to us in the high single digits on aggregate net sales for seltorexant products sold by the licensor outside the Minerva Territory. In accordance with the development agreement, we will pay 40% of seltorexant development costs related to the joint development of any seltorexant products.

Our share of aggregate development costs shall not exceed (i) $5.0 million for the period beginning from the effective date of the license and ending following the completion of certain Phase 1b clinical trials and animal toxicology studies, and (ii) $24.0 million for the period beginning from the effective date of the license and ending following the completion of certain Phase 2 clinical trials. Janssen has a right to opt out at the end of certain development milestones, after which, Janssen will not have to fund further development of seltorexant 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. 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.

We account for the co-development and license agreement as a joint risk-sharing collaboration in accordance with ASC 808, Collaboration Arrangements. Payments between us and the licensor with respect to each party's share of seltorexant development costs that have been incurred pursuant to the joint development plan are recorded within research and development expenses or general and administrative expenses, as applicable, in the accompanying consolidated statements of operations due to the joint risk-sharing nature of the activities. We have included zero and $2.5 million in accrued collaborative expenses, as of December 31, 2017

and December 31, 2016, respectively, related to this agreement. In the 12 months ended December 31, 2017 and 2016, we paid $2.5 million and zero, respectively, related to development activities under this agreement.

On July 6, 2016, we and Janssen agreed that "Decision Point 2" had been reached as defined under the co-development agreement. As neither party has exercised their right to withdraw from the agreement, we paid Janssen $3.5 million and incurred direct expenses of $0.3 million related to development activities under the current phase of development. During the 12 months ended December 31, 2017 and 2016, we recorded an expense of $11.2 million and $3.5 million, respectively, for certain development activities in accordance with the terms of the co-development agreement. We have included zero and $2.5 million in accrued collaborative expenses as of December 31, 2017 and December 31, 2016, respectively, related to this agreement.

In June 2017, we entered into the Amendment. The effectiveness of the Amendment was contingent upon approval of its terms by the European Commission and the closing of the acquisition of Actelion by affiliates of Janssen. These conditions were subsequently met, and the agreement became effective on August 29, 2017. Under the amended agreement, Janssen has waived its right to royalties on seltorexant insomnia sales in the European Union, Switzerland, Liechtenstein, Iceland and Norway (the "Minerva Territory"). We retain all of its rights to seltorexant, including commercialization of the molecule for the treatment of insomnia and as an as adjunctive therapy for MDD, which include an exclusive license in the Minerva Territory, with royalties payable by us to Janssen on seltorexant MDD sales. Royalties on sales outside of the Minerva Territory are payable by Janssen to us. Janssen made an upfront payment to us of $30 million upon the effectiveness of the Amendment and agreed to make a $20 million payment at the start of a Phase 3 insomnia trial for seltorexant and a $20 million payment when 50% of the patients are enrolled in this trial. Janssen further agreed to waive the remaining payments due from us until completion of the Phase 2 development of seltorexant. The $30 million payment and $11.2 million in previously accrued collaborative expenses, which were forgiven upon the effective date of the agreement, will be earned and recognized as revenue as the services are performed from the commencement of Phase 3 development to the completion of the development activities using the proportional performance method. The $30 million payment along with the $11.2 million in previously accrued collaborative expenses have been included under Deferred Revenue on our balance sheet at December 31, 2017. In connection with the Amendment, we repurchased all of the approximately 3.9 million shares of its common stock previously owned by Johnson & Johnson Innovation-JJDC Inc. at a per share price of $0.0001, for an aggregate purchase price of approximately $389.

As a result of the Amendment, we assumed strategic control for the clinical development of seltorexant in insomnia under the Phase 2 development program, but has no further financial obligations until the Phase 2b development milestone is complete, which is expected to occur in the second half of 2019. Upon completion of this development milestone, referred to as "Decision Point 4", Minerva has the right to opt-out of the agreement and collect a royalty on worldwide sales of seltorexant in the single digits with no further obligations to Janssen. If we elect to continue to Phase 3, we would be obligated to fund the clinical trials related to insomnia, and receive $40 million in milestone payments from Janssen, and would also be responsible for 40% of Janssen's development costs in their Phase 3 MDD program.

Competition

Roluperidone: 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, and cognitive symptoms. 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 currently approved drug therapies for positive symptoms and their side effect profiles, we believe these therapies are unlikely to be directly competitive with roluperidone, which is intended to target primarily negative symptoms and cognitive impairment. However, new drug therapies in addition to roluperidone are being developed to address the limitations of current therapies. Several 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. On Sept. 22, 2017, Allergan announced it had received a Refusal to File (RTF) letter from the FDA regarding their antipsychotic product, Vraylar. The FDA, according to Allergan's press-release, determined that the sNDA for the treatment of negative symptoms was not sufficiently complete

to permit a substantive review. Allergan has stated that the company is in the process of planning a meeting with the FDA, to respond to the issues, and to seek clarification of what information will be required.

Specific compounds under development that include negative symptoms as a target include Acadia Pharmaceuticals' Pimavanserin, a selective serotonin inverse agonist (SSIA) that is approved for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis. Other products in clinical development whose targets include negative symptoms (although not necessarily defined as a primary outcome of their clinical trials) are SyneuRx's NaBen and Avanir Pharmaceuticals' AVP-786.

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 marketed 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 in cognitive and sexual functions. 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 treatment-resistant depression (TRD) 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, Janssen's esketamine and Allergan's rapastinel (formerly Naurex GLYX-13) both target the NMDA receptor and are expected to have a faster onset of therapeutic effect as compared to currently available therapies.

Seltorexant: 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, seltorexant, 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 seltorexant's launch. If approved, we believe seltorexant, which is a single orexin receptor antagonist that targets orexin 2 pathways only and has a different pharmacokinetic profile from Belsomra, may 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. 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, which we own or are exclusively licensed to us, are summarized below.

Roluperidone

Compound

Under our agreement with MTPC, we have an exclusive license to U.S. Patent No. 7,166,617, which claims the roluperidone compound, as well as to corresponding patents in the following countries: Australia, Canada, Europe (Albania, Austria, Belgium, Republic of Cyprus, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Latvia, Liechtenstein, Lithuania, Luxembourg, Macedonia, Monaco, Netherlands, Portugal, Romania, Slovenia, Spain, Sweden, Switzerland, Turkey, and United Kingdom), Israel, New Zealand, and Russia.

The US '617 patent expires no earlier than May 17, 2021, and a patent term extension of up to 5 years may be available in the U.S. The foreign patents expire no earlier than February 26, 2021.

Pharmaceutical Compositions

We own a granted U.S. patent, a pending U.S. application and a corresponding PCT application which claim modified-release formulations of roluperidone. We plan to nationalize the PCT application in a number of foreign countries in the coming months. The terms of existing and any future granted patents in this patent family will expire no earlier than November 30, 2035.

Methods of Use

We own two granted patents in the U.S., Russia, and Europe (Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Norway, Poland, Portugal, Spain, Sweden, Switzerland, Turkey, and United Kingdom) and several pending applications in two patent families that are directed to methods of use of roluperidone to treat negative and other symptoms of schizophrenia, sleep disorders, depression and other sigma-2

disorders or conditions. Applications from these families are currently pending in the United States, Australia, Brazil, Canada, Europe and Russia. The terms of existing and any future granted patents in these two families will expire no earlier than July 20, 2031.

We also own a PCT application filed in 2017, which is directed to the use of roluperidone to treat negative symptoms in non-schizophrenic patients. We plan to file a national phase application in late 2018 from this PCT application.

MIN-117

Compound

Under our agreement with MTPC, we have an exclusive license to U.S. Patent No. 6,720,320, which claims the MIN-117 compound, as well as to corresponding patents in the following countries: Canada and Europe (Germany, France, Italy, Netherlands, Spain and United Kingdom). The U.S. ‘320 patent expires no earlier than August 13, 2020, and a patent term extension of up to 5 years may be available in the U.S. The foreign patents expire no earlier than May 22, 2020.

Pharmaceutical Compositions and Methods of Use

We own pending applications in a patent family that are directed to compositions comprising a low dose of MIN-117 and their use for treating depression, sleep disorders and improving cognitive impairment in patients with depression. The applications we own are pending in the United States, Europe, Australia, Brazil, Canada, Chile, Colombia, Israel, Mexico, New Zealand, Peru, Russia, and South Africa. Patents that grant from these applications will expire no earlier than January 24, 2034. A patent term extension of up to five years may be available in the United States.

We also own a PCT application filed in 2017, which is directed to the use of MIN-117 to treat anxiety disorders. We plan to file national phase applications in 2018 from this patent application.

Seltorexant

Compound

Under our agreement with Janssen, we are an exclusive licensee of European Patent EP2491038, which claims the seltorexant compound and was validated in 39 European countries. The terms of these patents will expire no earlier than October 21, 2030.

Methods of Use

We also have rights to a U.S. provisional patent application filed in 2016, which is directed to the use of seltorexant to treat depression.

MIN-301

We own a patent family that is directed to the use of MIN-301 for treating neurologic and psychiatric diseases, including Parkinson’s disease. This patent family includes patents granted in Australia, Europe (Austria, Belgium, Denmark, France, Germany, Greece, Ireland, Italy, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, Turkey and United Kingdom), Japan, Mexico and Russia. Applications are pending in the United States, Canada, China, Hong Kong and Mexico. The term of existing and any future granted patents in this family will expire no earlier than November 17, 2028. A patent term extension of up to five years may be available in the United States.

Data and Marketing Exclusivity

In addition to patent protection, our product candidates may also be eligible for data and marketing exclusivity protection in the U.S., EU and certain other countries. If this protection is available, no competitor may use the data in our marketing application to obtain marketing approval of a generic product during the exclusivity period.

For small molecules, such as roluperidone, seltorexant and MIN-117, the data and marketing exclusivity period is generally five years in the U.S. and ten years in the EU, measured from the FDA and EU approval dates, respectively. If MIN-301 is approved as a biologic product, it may be eligible for a data and marketing exclusivity period of twelve years in the U.S. and ten years in the EU. The data and marketing exclusivity periods in the U.S. and EU may be extended by 6 months of pediatric exclusivity if a qualifying pediatric study is performed.

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 expanded our internal capabilities related to commercial planning, strategic product development and product marketing during the fourth quarter of 2017 as we plan the establishment of a sales, marketing and product distribution infrastructure in the future. Except for most of Asia, we have global commercialization rights for two of our product candidates, roluperidone and MIN-117, and European Union commercialization rights for seltorexant. We have worldwide rights for MIN-301. We believe that it will be possible for us to access European and, in the case of roluperidone, MIN-117 and MIN-301, other priority markets including the United States,

Asia, and Latin America, through a focused, specialized sales 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. Additionally, we plan to engage fully with all key constituencies involved in treatment decisions, including payors, patients and others.

Government Regulation and Product Approval

Clinical Trials and Marketing Authorization in the European Union

In Europe, a clinical trial application, or CTA, must currently 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. Under the new Regulation on Clinical Trials, which is expected to take effect in 2019, there will be a centralized application procedure where one national authority takes the lead in reviewing the application and the other national authorities have only a limited involvement. Any substantial changes to the trial protocol or other information submitted with the clinical trial applications must be notified to or approved by the relevant competent authorities and ethics committees. In all cases, the clinical trials must be conducted in accordance with good clinical practices and other applicable regulatory requirements and medicines used in clinical trials must be manufactured in accordance with good manufacturing practices. 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, collectively referred to herein as the EEA. Submission of one MAA thus leads to one assessment process and one authorization that allows access to the market of the entire EEA. 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. Under the centralized procedure, the maximum timeframe for the evaluation of an MAA by the EMA is 210 days. This excludes so-called clock stops, during which

additional written or oral information is to be provided by the applicant in response to questions asked by the Committee for Human Medicinal Products, or CHMP. At the end of the review period, the CHMP provides an opinion to the European Commission. If this is opinion favorable, the Commission may then adopt a decision to grant a marketing authorization. In exceptional cases, the CHMP might perform an accelerated review of an MAA in no more than 150 days. This is usually when the product is of major interest from the point of view of public health and, in particular, from the viewpoint of therapeutic innovation.

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.

The European Union medicines rules expressly permit the EU Member States to adopt national legislation prohibiting or restricting the sale, supply or use of any medicinal product containing, consisting of or derived from a specific type of human or animal cell, such as embryonic stem cells. While the products we have in development do not make use of embryonic stem cells, it is possible that the

national laws in certain EU Member States may prohibit or restrict us from commercializing our products, even if they have been granted an EU marketing authorization.

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 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 deferral or waiver applies 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. MIN-301, a peptide, may be regulated as a biologic and additionally subject to the Public Health Service Act. 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 allow pending Investigational New Drug Applications, or INDs, and approve NDAs, withdrawal of a marketing approval, imposition of clinical holds or termination of clinical trials, or issuance of Warning 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 sponsor of an approved application is also subject to annual program 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.

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

In the European Union, holders of a marketing authorization must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance, or QPPV, who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports, or PSURs.

All new European marketing authorization applications must include a risk management plan, or RMP, describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the marketing authorization. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies. RMPs and PSURs are routinely available to third parties requesting access, subject to limited redactions. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the European Union. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each EU Member State and can differ from one country to another.

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, individual imprisonment, exclusion from participation in government healthcare programs, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, 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 federal and proposed and enacted state legislation 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. At the federal level, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

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, or collectively, the ACA, which substantially changed healthcare financing and delivery by both governmental and private insurers, and significantly impacted the pharmaceutical industry. The ACA contains provisions that may potentially reduce the profitability of products, including, for example, increased rebates for products sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. There have been judicial and congressional challenges to the ACA, as well as efforts by the Trump administration to repeal or replace certain aspects of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law, including the repeal, effective January 1, 2019, of the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate" and delays in the implementation of the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on imposed on certain non-exempt medical devices. Congress could still consider other legislation to repeal or repeal and replace all or portions of the ACA. Congress could still consider other legislation to repeal or repeal and replace all or portions of the ACA. We expect that healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and lower reimbursement, and in additional downward pressure on the price that may be charged for any of our product candidates, if approved.

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.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as ''Brexit''. Thereafter, on March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The withdrawal of the United Kingdom from the European Union is expected to take effect either on the effective date of the withdrawal agreement to be negotiated by the parties or, in the absence of agreement, two years after the United Kingdom provided the notice of withdrawal pursuant to the Treaty on European Union, or on March 29, 2019. Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, immediately following Brexit, it is expected that the United Kingdom's regulatory regime will remain aligned to European regulations. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the United Kingdom. In the longer term, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom.

Employees

As of December 31, 2017, we had 12 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 year ended December 31, 2017, and 2016, we reported net losses of $31.5 million and $31.0 million, respectively. As of December 31, 2017, we had an accumulated deficit of $164.4 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, 2017, we had cash, cash equivalents and marketable securities (current and non-current) of $133.2 million. We believe that our existing cash, cash equivalents and marketable securities (current and non-current) will be sufficient to meet our cash commitments for at least the next 12 months after the date that the year-end condensed financial statements are issued. The process of drug development can be costly and the timing and outcomes of clinical trials is uncertain. The assumptions upon which we have based our estimates are routinely evaluated and may be subject to change. The actual amount of our expenditures will vary depending upon a number of factors including but not limited to the design, timing and duration of future clinical trials, the progress of our research and development programs and the level of financial resources available.

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.

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

On December 22, 2017, President Trump signed into law new legislation that significantly revises the Internal Revenue Code of 1986, as amended (the “Code”). The newly enacted federal income tax law, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings

(except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain if and to what extent various states will conform to the newly enacted federal tax law.

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, 2017, we had approximately $64.8 million of Federal NOL carryforwards. These Federal NOL carryforwards will begin to expire at various dates beginning in 2027, if not utilized. Under the newly enacted Federal income tax law, Federal NOLs incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such Federal NOLs is limited. 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. If substantial changes in ownership have occurred, there could be annual limitations on the amount of carryforwards that can be realized in future periods. 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, the concurrent private placements or our subsequent public offerings. 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 Code. Further, state NOL carryforwards may be similarly limited. We had approximately $56.3 million of state net operating carryforwards at December 31, 2017. 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, or Biologics License Application, or BLA, 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 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 3 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, roluperidone 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 2, 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 2, 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 roluperidone 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 statistically significant efficacy of the product candidate studied for the target indication in later stages of clinical development. For example, although we believe our Phase 2b trial with roluperidone met its primary endpoint as we observed the statistically significant benefit of roluperidone over placebo in improving negative symptoms in patients with schizophrenia, we must conduct pivotal, Phase 3 trials with roluperidone that may fail to demonstrate safety and efficacy. Our Phase 2a trial with MIN-117, while we observed a reduction in depressive symptoms, was designed to detect a signal of efficacy and not to demonstrate statistically significant differences between MIN-117 and placebo. Further clinical trials with MIN-117 will need to be statistically powered to demonstrate such differences. Regulatory authorities may find that our 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 roluperidone 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, roluperidone 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, roluperidone. As a result, we may forego or delay pursuit of opportunities

with other product candidates, including MIN-117, seltorexant 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;
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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.

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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 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 seltorexant, 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 a limited marketing and sales organization. If we are unable to establish greater 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 have a limited 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 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 and other third-party payors, such as private health insurers and health maintenance organizations. Government authorities and other third-party payors, 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.

We cannot be sure that coverage and reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Coverage and reimbursement may impact the demand for, or the price of, any

product candidate for which we obtain marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the EMA, FDA or comparable foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may only be temporary. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Prices paid for a drug also vary depending on the class of trade. Prices charged to government customers and certain customers that receive federal funds are subject to price controls, and private institutions may obtain discounts through group purchasing organizations or use formularies to leverage discounts. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States.

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 federal and proposed and enacted state legislation 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. At the federal level, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Our inability to promptly obtain coverage and profitable reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Recently enacted and future legislation may increase the difficulty and cost for us to commercialize our product candidates and affect the prices we may obtain.

In the United States and many foreign jurisdictions, the legislative landscape continues to evolve. There have been a number of enacted or proposed legislative and regulatory changes affecting the healthcare system and pharmaceutical industry that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidate for which we obtain marketing approval.

For example, in March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or, collectively, the ACA, a law intended to, among other things, broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against healthcare fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on pharmaceutical and medical device manufacturers and impose additional health policy reforms. Some of the provisions of the ACA have yet to be implemented, and there have been judicial and congressional challenges to certain aspects of the ACA, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the ACA. Since January 2017, President Trump has signed two

Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate”. Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called “Cadillac” tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax imposed on certain non-exempt medical devices. Congress could still consider other legislation to repeal or repeal and replace all or portions of the ACA. We continue to evaluate the effect that the ACA and its possible repeal and replacement has on our business. We cannot predict the full impact of the ACA on pharmaceutical companies, as many of the ACA reforms require the promulgation of detailed regulations implementing the statutory provisions, which has not yet occurred.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenue, if any.

In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. In some countries, particularly in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a health technology assessment that compares the cost-effectiveness of our drug candidate to other available therapies. There can be no assurance that our products will be considered cost-effective, that an adequate level of reimbursement will be available or that a foreign country's reimbursement policies will not adversely affect our ability to sell our products profitably.

If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

Our international operations are subject to foreign currency and exchange rate risks.

Because we plan to continue to conduct our clinical trials in Europe, we are exposed to currency fluctuations and exchange rate risks. The costs of our CROs may be incurred in Euros and we may pay them in Euros, however, we expect to keep the substantial portion of our cash, cash equivalents, marketable securities (current and non-current) and private placement transactions, in United States Dollars. Therefore, fluctuations in foreign currencies, especially the Euro, could significantly impact our costs of conducting clinical trials. In addition, we may have to seek additional funding earlier than expected, which may not be available on acceptable terms or at all. Changes in the applicable currency exchange rates might negatively affect the profitability and business prospects of the third parties conducting our future clinical trials. This might cause such third parties to demand higher fees or discontinue their operations. These situations could in turn increase our costs or delays our clinical development, which could have a material adverse effect on our business, financial condition and results of operations.

A variety of risks associated with international operations could materially adversely affect our business.

We expect to engage in significant cross-border activities, and we will be subject to risks related to international operations, including:

- different regulatory requirements for maintaining approval of drugs in foreign countries;
- reduced protection for contractual and intellectual property rights in certain countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in North America;
- tighter restrictions on privacy and the collection and use of patient data; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

If any of these issues were to occur, our business could be materially harmed.

If we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, scientific and medical personnel, especially Dr. Remy Luthringer, whose services are critical to the successful implementation of our product candidate development and regulatory strategies. We do not maintain “key man” insurance policies on the lives of these individuals or the lives of any of our other employees. In order to induce valuable employees to continue their employment with us, we have provided stock options that vest over time. The value to employees of stock options that vest over time is significantly affected by movements in our stock price that are beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies.

Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us on short notice. Pursuant to their employment arrangements, each of our executive officers may voluntarily terminate their employment at any time by providing as little as thirty days advance notice. Our employment arrangements, other than

those with our executive officers, provide for at-will employment, which means that any of our employees (other than our executive officers) could leave our employment at any time, with or without notice. The loss of the services of any of our executive officers or other key employees and our inability to find suitable replacements could potentially harm our business, financial condition and prospects. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level, and senior managers as well as junior, mid-level, and senior scientific and medical personnel.

We may not be able to attract or retain qualified management and scientific personnel in the future due to the intense competition for a limited number of qualified personnel among biopharmaceutical, biotechnology, pharmaceutical and other businesses. Many of the other pharmaceutical companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high quality candidates than what we have to offer. If we are unable to continue to attract and retain high quality personnel, the rate and success at which we can develop and commercialize product candidates will be limited.

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

As of December 31, 2017, we had twelve full-time employees. As our development and commercialization plans and strategies develop, we expect to need additional managerial, operational, sales, marketing, financial and other resources. Future growth would impose significant added responsibilities on members of management, including:

- managing our clinical trials effectively;
- identifying, recruiting, maintaining, motivating and integrating additional employees;
- managing our internal development efforts effectively while complying with our contractual obligations to licensors, licensees, collaborators, contractors and other third parties;
- improving our managerial, development, operational and finance systems; and
- developing our compliance infrastructure and processes to ensure compliance with complex regulations and industry standards regarding us and our product candidates.

As our operations expand, we expect that we will need to manage additional relationships with various strategic partners, collaborators, suppliers and other third parties. Our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our development efforts and clinical trials effectively and hire, train and integrate additional management, administrative and sales and marketing personnel. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing our company.

We are party to a loan and security agreement that contains operating and financial covenants that may restrict our business and financing activities.

On January 16, 2015, we entered into a Loan and Security Agreement with Oxford Finance LLC and Silicon Valley Bank, providing for term loans to us in an aggregate principal amount of up to $15 million, in two tranches of $10 million and $5 million, respectively. We borrowed the first tranche in January 2015. In June 2016, we irrevocably elected not to borrow the additional $5 million available under the term loans. Borrowings under this loan and security agreement are secured by substantially all of our assets, excluding certain intellectual property rights. The loan and security agreement restricts our ability, among other things, to:

- sell, transfer or otherwise dispose of any of our business or property, subject to limited exceptions;
- make material changes to our business or management;

- enter into transactions resulting in significant changes to the voting control of our stock;
- make certain changes to our organizational structure;
- consolidate or merge with other entities or acquire other entities;
- incur additional indebtedness or create encumbrances on our assets;
- pay dividends, other than dividends paid solely in shares of our common stock, or make distributions on and, in certain cases, repurchase our stock;
- enter into transactions with our affiliates;
- repay subordinated indebtedness; or
- make certain investments.

In addition, we are required under our loan agreement to comply with various affirmative operating covenants. The operating covenants and restrictions and obligations in our loan and security agreement, as well as any future financing agreements that we may enter into, may restrict our ability to finance our operations, engage in business activities or expand or fully pursue our business

strategies. Our ability to comply with these covenants may be affected by events beyond our control, and we may not be able to meet those covenants. A breach of any of these covenants could result in a default under the loan and security agreement, which could cause all of the outstanding indebtedness under the facility to become immediately due and payable and eliminate our eligibility to receive additional loans under the agreement.

If we are unable to generate sufficient cash available to repay our debt obligations when they become due and payable, either as when such obligations become due, when they mature, or in the event of a default, we may not be able to obtain additional debt or equity financing on favorable terms, if at all, which may negatively impact our business operations and financial condition.

Future acquisitions, mergers or joint ventures could disrupt our business and otherwise harm our business.

We actively evaluate various strategic transactions on an ongoing basis and may acquire other businesses, products or technologies as well as pursue strategic alliances, joint ventures or investments in complementary businesses. We merged with Sonkei in November 2013 and acquired Mind-NRG in February 2014, but otherwise do not have any substantial experience integrating or managing acquired businesses or assets. Strategic transactions expose us to many risks, including:

- disruption in our relationships with collaborators or suppliers as a result of such a transaction;
- unanticipated liabilities related to acquired companies;
- difficulties integrating acquired personnel, technologies and operations into our existing business;
- retention of key employees;
- diversion of management time and focus from operating our business to management of strategic alliances or joint ventures or acquisition integration challenges;
- increases in our expenses and reductions in our cash available for operations and other uses; and
- possible write-offs or impairment charges relating to acquired businesses.

Foreign acquisitions, such as the acquisition of Mind-NRG, a Swiss company, involve unique risks in addition to those mentioned above, including those related to integration of operations across different cultures and languages, currency risks and the particular economic, political and regulatory risks associated with specific countries.

Also, the anticipated benefit of any strategic alliance, joint venture or acquisition may not materialize. Future acquisitions or dispositions could result in potentially dilutive issuances of our equity securities, the incurrence of debt (including on terms that are unfavorable to us that we are unable to repay or that may place burdensome restrictions on our operations), contingent liabilities or amortization expenses or write-offs of goodwill, any of which could harm our financial condition. We cannot predict the number, timing or size of future joint ventures or acquisitions, or the effect that any such transactions might have on our operating results.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranties brought by subjects enrolled in our clinical trials, patients, healthcare providers or others using, administering or selling our products. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates, if approved. Even successful defense would require significant financial and management resources.

Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our product candidates or products that we may develop;
- termination of clinical trial sites or entire trial programs;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling revisions, marketing or promotional restrictions;

- loss of revenues from product sales; and
- the inability to commercialize our product candidates.

Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. We do not currently carry any product liability insurance. Although we anticipate obtaining and maintaining such insurance in line with our needs for our upcoming trials, such insurance may be more costly than we anticipate and any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by such insurance or that is in excess of the limits of such insurance coverage. We also expect our insurance policies will also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

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

Despite the implementation of security measures, our internal computer systems and those of our CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial condition, results of operations or cash flows, which may adversely affect investor confidence in us and, as a result, the value of our common stock.

We are required to comply with the SEC's rules that implement Section 404 of the Sarbanes-Oxley Act and the Committee on Sponsoring Organizations, or COSO, Report on Internal Control – Integrated Framework, which require, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. Under Section 404 of the Sarbanes-Oxley Act, we are required to furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting. This assessment must include disclosure of any material weaknesses identified by management in our internal control over financial reporting. A material weakness is a control deficiency, or combination of control deficiencies, in internal control over financial reporting that results in more than a reasonable possibility that a material misstatement of annual or interim financial statements will not be prevented or detected on a timely basis. Further, in our first annual report required to be filed with the SEC following the date we are no longer an "emerging growth company," as defined in the JOBS Act, our independent registered public accounting firm will be required to attest to the effectiveness of our internal control over financial reporting.

Our compliance with Section 404 requires that we compile the system and process documentation necessary to perform an appropriate evaluation. During the evaluation and testing process, if we identify one or more material weaknesses in our internal control over financial reporting, we will be unable to assert that our internal control over financial reporting is effective. While we have established certain procedures and control over our financial reporting processes, we cannot assure you that these efforts will prevent restatements of our financial statements in the future. If we identify any future significant deficiencies or material weaknesses, the accuracy and timing of our financial reporting may be adversely affected and we may be unable to maintain compliance with securities law requirements

regarding timely filing of periodic reports. In addition, investors' perceptions that our internal controls are inadequate or that we are unable to produce accurate financial statements on a timely basis may harm our stock price and business prospects. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to the periodic reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act. We designed our disclosure controls and procedures to reasonably assure us that the information we disclose in reports we file in accordance with the Exchange Act is accurate, complete, reviewed by management and reported within the required time period. We believe that any disclosure controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

Prior to November 2013, we operated without full time employees, relying on the services of consultants, including representatives of our former affiliate, Care Capital LLC, to provide certain accounting and finance functions. We have since hired personnel and continue to develop our disclosure control procedures; however, if we are unsuccessful in building an appropriate infrastructure, or unable to develop procedures and controls to ensure timely and accurate reporting, we may be unable to meet our disclosure requirements under the Exchange Act, which could adversely affect the market price of our common stock and impair our access to the capital markets.

Our employees, independent contractors, principal investigators, CROs, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees and independent contractors, such as principal investigators, CROs, manufacturers, consultants, commercial partners and vendors, could include failures to comply with EMA or FDA regulations, to provide accurate information to the FDA, to comply with manufacturing standards we have established, to comply with European, federal and state healthcare fraud and abuse laws, to report financial information or data accurately or to disclose unauthorized activities to us. In particular, sales, marketing and other business arrangements in the healthcare industry are subject to extensive laws intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws may restrict or prohibit a wide range of business activities, including, but not limited to certain activities related to research, manufacturing, distribution, pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee and independent contractor misconduct could also involve the improper use of individually identifiable information, including, without limitation, information obtained in the course of clinical trials, which could result in sanctions, monetary penalties, and serious harm to our reputation. In addition, federal procurement laws impose substantial penalties for misconduct in connection with government contracts and require certain contractors to maintain a code of business ethics and conduct.

We have adopted a code of business ethics and conduct, but it is not always possible to identify and deter employee and independent contractor misconduct, and the precautions we take to detect and prevent improper activities may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, disgorgement, individual imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, diminished profits and future earnings and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate.

Any relationships with healthcare professionals, principal investigators, consultants, customers (actual and potential) and third-party payors in connection with our current and future business activities may and may continue to be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, marketing expenditure tracking and disclosure (or "sunshine") laws, government price reporting, and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face penalties, contractual damages, reputational harm, diminished profits and future earnings and curtailment or restructuring of our operations.

Our business operations and activities may be directly, or indirectly, subject to various federal, state and local healthcare laws, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act. These laws may impact, among other things, our current activities with principal investigators and research subjects, as well as proposed and future sales, marketing and education programs. In addition, we may be subject to patient data privacy and security regulation by the federal government, state governments and foreign jurisdictions in which we conduct our business. The healthcare laws and regulations that may affect our ability to operate include, but are not limited to:

- The federal Anti-Kickback Statute, which prohibits, among other things, individuals and entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, the referral of an individual for the furnishing or arranging for the furnishing of any item or service, or the purchase, lease, order, arrangement for, or recommendation of the purchase, lease, or order of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs.
- The federal civil False Claims Act, which imposes civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent; knowingly making, using or causing to be made or used, a false record or statement to get a false or fraudulent claim paid or approved by the government; conspiring to defraud the government by getting a false or fraudulent claim paid or approved by the government; or knowingly making, using or causing to be made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government.
- 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.
- The civil monetary penalties statute, which imposes penalties against any person or entity who, 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.
- The Veterans Health Care Act of 1992 that requires manufacturers of "covered drugs" to offer them for sale to certain federal agencies, including but not limited to, the Department of Veterans Affairs, on the Federal Supply Schedule, which requires compliance with applicable federal procurement laws and regulations and subjects manufacturers to contractual remedies as well as administrative, civil and criminal sanctions.
- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private), knowingly and willfully embezzling or stealing from a health care benefit program, willfully obstructing a criminal investigation of a health care offense and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters.
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans and healthcare clearinghouses as well as their respective business associates that perform

services for them that involve individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization, including mandatory contractual terms as well as directly applicable privacy and security standards and requirements.

- The federal Physician Payments Sunshine Act and its implementing regulations requires manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the United States Department of Health and Human Services, or HHS, information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members.
- Federal consumer protection and unfair competition laws, which broadly regulate marketplace and other activities that potentially harm consumers.

- State law equivalents of each of the above federal laws, such as anti-kickback, false claims, consumer protection and unfair competition laws which may apply to our business practices, including but not limited to our research, distribution, sales and marketing arrangements and our practices for submitting claims involving healthcare items or services reimbursed by any third-party payors, including commercial insurers. State laws may also (1) require that pharmaceutical companies comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government that otherwise restrict the payments that may be made to healthcare providers, (2) require that drug manufacturers file reports with states regarding marketing information, such as the tracking and reporting of gifts, compensations and other remuneration and items of value provided to healthcare professionals and entities (compliance with such requirements may require investment in infrastructure to ensure that tracking is performed properly, and some of these laws result in the public disclosure of various types of payments and relationships, which could potentially have a negative effect on a pharmaceutical company's business and/or increase enforcement scrutiny of its activities) and (3) govern the privacy and security of health information in certain circumstances. State laws are not uniform, may differ from each other in significant ways and may be applied with differing effects.

In addition, any sales of our products or product candidates once commercialized outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws such as, for instance, the UK Bribery Act 2010 other national anti-corruption legislation made as a consequence of a member states' adherence to the OECD Convention on Combating Bribery of Foreign Public Officials in International Business Transactions, the European Union data protection regime set out in Directive 95/46/EC as implemented nationally by the member states, and European Union consumer laws protecting against defective products, including Directive 85/374/EEC. In addition, there are national laws and codes which are comparable to the United States "sunshine laws," including certain provisions under the UK ABPI Code of Practice and French disclosure requirements on manufacturers to publicly disclose interactions with French health care professionals.

Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws. If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to, without limitation, civil, criminal and administrative penalties, damages, monetary fines, disgorgement, individual imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate.

We are subject to the Foreign Corrupt Practices Act.

The Foreign Corrupt Practices Act, or FCPA, is a United States law that generally prohibits covered entities and their intermediaries from engaging in bribery or making other prohibited payments, offers or promises to foreign officials for the purpose of obtaining or retaining business or other advantages. In addition, the FCPA imposes recordkeeping and internal controls requirements on publicly traded corporations and their foreign affiliates, which are intended to, among other things, prevent the diversion of corporate funds to the payment of bribes and other improper payments, and to prevent the establishment of "off books" slush funds from which such improper payments can be made.

We and our service providers are subject to EU data protection laws. Failure to comply with such laws could harm our financial condition and operating results and involve distraction from other aspects of our business.

In October 2015, the Court of Justice of the European Union (CJEU) invalidated the EU-U.S. Safe Harbor Framework, which had established a means for legitimating the transfer of personal data, as the term is used in the

context of the EU Data Protection Directive, to the U.S. and required U.S.-based companies that have certified with the Department of Commerce as part of the Safe Harbor Framework to provide assurance that they are adhering to relevant European standards for data protection. As Minerva is not Safe Harbor certified, the CJEU's ruling invalidating the Safe Harbor has no direct effect on Minerva's own compliance with EU data protection laws; however, in light of the CJEU's recent decision, we are reviewing the practices of third party service providers with whom we work, which include the transfer of personal data between the European Economic Area ("EEA") and the U.S. to ensure that all data transfers to us comply with EU data protection laws. In February 2016, the EU Commission announced that it had reached agreement with the U.S. replacement regime to the Safe Harbor Framework, which is expected to be ratified in the EU in the next three to four months. We require our EEA-based services providers, and U.S.-based service providers undertaking clinical trials on our behalf in the EEA, to confirm that all of the personal data which we receive from them is legitimately transferred to us. In many cases we believe that patients and subjects consent to the transfer of their data in a manner which satisfies the requirements of EU data protection law. Where appropriate and pending the ratification of the replacement regime, we may require third party service providers to adopt an alternative means of legitimizing data transfers from the EEA, such as the Standard Contractual Clauses which

have been approved by the EU Commission as a means of transferring data to the U.S. These confirmations and, if necessary, additional actions may involve substantial time and expense to both Minerva and its third party service providers, and could divert management's attention and resources from other aspects of our business. If data transfers to the U.S. are not legitimized, the EU data protection authorities can impose a number of different sanctions, including fines and, ultimately, a prohibition on transfers, any of which could harm our business, financial condition and operating results.

Risks Related to Our Dependence on Third Parties

We currently rely and continue to expect to rely on third parties to conduct our future clinical trials. The failure of these third parties to successfully carry out their contractual duties or meet expected deadlines could substantially harm our business because we may not obtain regulatory approval for or commercialize our product candidates in a timely manner or at all.

We plan to rely upon third-party CROs to monitor and manage data for our future clinical programs. We will rely on these parties for execution of our clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with current GCPs, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for all of our products in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCP, the clinical data generated in our clinical trials may be deemed unreliable and the EMA, FDA or comparable regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements. In addition, we must conduct our clinical trials with product produced under cGMP requirements. Failure to comply with these regulations may require us to repeat pre-clinical and clinical trials, which would delay the regulatory approval process.

Our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical, nonclinical and pre-clinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. If necessary, switching or adding CROs involves substantial cost and requires extensive management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, prospects, financial condition and results of operations.

If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated, we may need to conduct additional trials, and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed. To the extent we are unable to successfully identify and manage the performance of third-party service providers in the future, our business may be adversely affected.

We contract with third parties for the manufacturing of our product candidates for pre-clinical and clinical testing and expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products, or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not have any manufacturing facilities. For our product candidates, we rely, and expect to continue to rely, on third parties for the manufacturing of our drug candidates for pre-clinical and clinical testing, as well as for commercial manufacture if any of our drug candidates receive marketing approval. This reliance on third parties increases the risk that we will not have sufficient quantities of our drug candidates or drugs, or such quantities at an acceptable cost or quality, which could delay, prevent or impair our ability to timely conduct our clinical trials or our other development or commercialization efforts.

We also expect to rely on third-party manufacturers or third-party collaborators for the manufacturing of commercial supply of any other drug candidates for which we or our collaborators obtain marketing approval. We may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how;
- disruption and costs associated with changing suppliers, including additional regulatory filings; and
- the possible termination or non-renewal of the agreement by the third party at a time that is costly or inconvenient for us.

Moreover, the facilities used by our contract manufacturers to manufacture our products must be approved by the FDA pursuant to inspections that will be conducted after we submit our marketing application to the FDA. Other national regulatory authorities have comparable powers. While we are ultimately responsible for the manufacture of our product candidates, other than through our contractual arrangements, we do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with cGMP requirements, for manufacture of both active drug substances and finished drug products. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other regulatory authorities, we will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, other than through our contractual agreements, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain marketing approval for or market our product candidates, if approved.

Further, our suppliers are subject to regulatory requirements, covering manufacturing, testing, quality control, and record keeping relating to our product candidates, and subject to ongoing inspections by the regulatory agencies. Failure by any of our suppliers to comply with applicable regulations may result in long delays and interruptions to our manufacturing capacity while we seek to secure another supplier that meets all regulatory requirements, as well as market disruption related to any necessary recalls or other corrective actions.

Third-party manufacturers may not be able to comply with cGMP, regulations or similar regulatory requirements outside the United States. Additionally, our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical hold or termination, fines, imprisonment, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures, refusal to allow product import or export, Warning Letters, Untitled Letters, or recalls of drug candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our drugs.

Our drug candidates and any drugs that we may develop may compete with other drug candidates and drugs for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply or a second source for bulk drug substance. If our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers and we may incur added costs and delays in identifying and qualifying any such replacement.

Our current and anticipated future dependence upon others for the manufacturing of our drug candidates or drugs may adversely affect our future profit margins and our ability to commercialize any drugs that receive marketing approval on a timely and competitive basis.

If our third-party manufacturers use hazardous and biological materials in a manner that causes injury or violates applicable law, we may be liable for damages.

Our research and development activities involve the controlled use of potentially hazardous substances, including chemical and biological materials, by our third-party manufacturers. Our manufacturers are or will be subject to federal, state and local laws in the United States and in Europe governing the use, manufacture, storage, handling and disposal of medical, radioactive and hazardous materials. Although we believe that our manufacturers' procedures for using, handling, storing and disposing of these materials comply with legally prescribed standards, we cannot completely eliminate the risk of contamination or injury resulting from medical, radioactive or hazardous materials. As a result of any such contamination or injury, we may incur liability or local, city, state, federal authorities or other equivalent national authorities may curtail the use of these materials and interrupt our business operations. In the event of an accident, we could be held liable for damages or penalized with fines, and the liability could exceed our resources. We do

not have any insurance for liabilities arising from medical radioactive or hazardous materials. Compliance with applicable environmental laws is expensive, and current or future environmental regulations may impair our research, development and production efforts, which could harm our business, prospects, financial condition or results of operations.

We may engage third party collaborators to market and commercialize our product candidates, who may fail to effectively commercialize our product candidates.

We may utilize strategic partners or contract sales forces, where appropriate, to assist in the commercialization of our product candidates, if approved. We currently possess limited resources and may not be successful in establishing collaborations or co-promotion arrangements on acceptable terms, if at all. We also face competition in our search for collaborators and co-promoters. By entering into strategic collaborations or similar arrangements, we will rely on third parties for financial resources and for development, commercialization, sales and marketing and regulatory expertise. Any collaborators may fail to develop or effectively commercialize our product candidates because they cannot obtain the necessary regulatory approvals, they lack adequate financial or other resources or they decide to focus on other initiatives. Any failure to enter into collaboration or co-promotion arrangements or the failure of our third party collaborators to successfully market and commercialize our product candidates would diminish our revenues and harm our results of operations. In addition, conflicts may arise with our collaborators, such as conflicts concerning the interpretation of clinical data, the achievement of milestones, the interpretation of financial provisions or the ownership of intellectual property. If any conflicts arise with our collaborators, they may act in their self-interest, which may be adverse to our best interest.

We depend on our collaborations with Mitsubishi Tanabe Pharma Corporation, or MTPC, and Janssen Pharmaceutica NV and could be seriously harmed if our license agreements with MTPC and Janssen were terminated.

We exclusively license roluperidone and MIN-117 from MTPC, with the rights to develop, sell and import roluperidone and MIN-117 globally, excluding most of Asia.

Our co-development and license agreement with Janssen provides us with European Union commercialization rights for seltorexant and the right to royalties on any sales of seltorexant outside of the European Union. We have assumed strategic control for clinical development of seltorexant in insomnia and all financial responsibility for Phase 3 development costs for seltorexant in this indication and will only realize revenues from seltorexant if it is approved and if our license agreement with Janssen is not terminated by Janssen. Janssen may terminate our license agreement following a material breach by us or certain insolvency events, including if we are unable to fund our portion of the development costs. As a result, we may never realize any revenues from the commercialization of seltorexant, even if approved. In addition, at certain development milestones, including the completion of a single dose Phase 1 clinical trial of seltorexant in patients with MDD, Janssen has the right to opt out of its obligation to fund further development, and we may be unable to fund such development without Janssen's financial support.

Even if we receive revenues on European Union sales or royalties on sales outside of the European Union under the Janssen license agreement, we may not receive revenues that equal or exceed the amount we are obligated to invest in seltorexant's clinical development under the agreement. As a result, the license agreement for seltorexant may never result in any profits to us and may have a material adverse effect on us or our business prospects.

We may not be successful in establishing new collaborations which could adversely affect our ability to develop future product candidates and commercialize future products.

We are collaborating with Janssen on the development of seltorexant. We may also seek to enter into additional product collaborations in the future, including alliances with other biotechnology or pharmaceutical companies, to

enhance and accelerate the development of our future product candidates and the commercialization of any resulting products. We face significant competition in seeking appropriate collaborators and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish collaborations or other alternative arrangements for any future product candidates because our research and development pipeline may be insufficient, our product candidates may be deemed to be at too early of a stage of development for collaboration efforts and/or third parties may view our product candidates as lacking the requisite potential to demonstrate safety and efficacy. As a result, we may have to delay the development of a product candidate and attempt to raise significant additional capital to fund development. Even if we are successful in our efforts to establish collaborations, the terms that we agree upon may not be favorable to us and we may not be able to maintain such collaborations if, for example, development or approval of a product candidate is delayed or sales of an approved product are disappointing.

Risks Related to Intellectual Property

If we are unable to obtain or protect intellectual property rights, we may not be able to compete effectively in our market.

Our success depends in significant part on our and our licensors', licensees' or collaborators' ability to establish, maintain and protect patents and other intellectual property rights and operate without infringing the intellectual property rights of others. We have filed numerous patent applications both in the United States and in foreign jurisdictions to obtain patent rights to inventions we have discovered. We have also licensed from third parties rights to patent portfolios. None of these licenses give us the right to prepare, file and prosecute patent applications and maintain patents we have licensed, although we may provide comments on prosecution matters, which our licensors may or may not choose to follow. If our licensors elect to discontinue prosecution or maintenance of our licensed patents, we have the right, at our expense, to pursue and maintain those patents and applications.

The patent prosecution process is expensive and time-consuming, and we and our current or future licensors, licensees or collaborators may not be able to prepare, file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we or our licensors, licensees or collaborators will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from or license to third parties and are reliant on our licensors, licensees or collaborators. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. If our current or future licensors, licensees or collaborators fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our licensors, licensees or collaborators are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. Because the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, issued patents that we own or have licensed from third parties may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in the loss of patent protection, the narrowing of claims in such patents or the invalidity or unenforceability of such patents, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection for our technology and products.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our and our current or future licensors', licensees' or collaborators' patent rights are highly uncertain. Our and our licensors', licensees' or collaborators' pending and future patent applications may not result in patents being issued that protect our technology or products, in whole or in part, or that effectively prevent others from commercializing competitive technologies and products. The patent examination process may require us or our licensors, licensees or collaborators to narrow the scope of the claims of our or our licensors', licensees' or collaborators' pending and future patent applications, which may limit the scope of patent protection that may be obtained. Our and our licensors', licensees' or collaborators' patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications, and then only to the extent the issued claims cover the technology.

One or more of our owned or licensed patents directed to our proprietary products or technologies may expire or have limited commercial life before the proprietary product or technology is approved for marketing in a relevant jurisdiction.

Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting our product candidates might expire before or shortly after our product candidates obtain regulatory approval, which may subject us to increased competition and reduce or eliminate our ability to recover our development costs. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. For example, our in-licensed U.S. and European patents covering composition of matter and pharmaceutical compositions of roluperidone, respectively, are expected to expire as soon as 2021. In addition, our in-licensed U.S. and European patents relating to pharmaceutical compositions and uses of MIN-117 to treat depression are expected to expire as soon as 2020. Finally, any patent that grants from our U.S. patent applications relating to methods of using MIN-301 to treat neurologic and psychiatric diseases is expected to expire as early as 2028. Although we expect to seek extensions of patent terms where available, including in the United States under the Drug Price Competition and Patent Term Restoration Act of 1984, which permits a patent term extension of up to five years beyond the expiration of the patent, we cannot be certain that an extension will be granted, or if granted, what the applicable time period or the scope of patent protection afforded during any extended period will be. The applicable authorities, including the EMA, FDA, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and pre-clinical data and launch their product earlier than might otherwise be the case.

The expiration of composition of matter patent protection with respect to one or more of our product candidates may diminish our ability to maintain a proprietary position for our intended uses of a particular product candidate. Moreover, we cannot be certain that we will be the first applicant to obtain an FDA approval for any indication of one or more of our product candidates and we cannot be certain that it will be entitled to new chemical entity, or NCE, exclusivity. Such diminution of our proprietary position could have a material adverse effect on our business, results of operations and financial condition.

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

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

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

Competitors may infringe our issued patents or other intellectual property. In some cases, it may be difficult or impossible to detect third-party infringement or misappropriation of our intellectual property rights, even in relation to issued patent claims, and proving any such infringement may be even more difficult. Accordingly, for such undetectable infringement or misappropriation our ability to recover damages will be negligible and we could be at a market disadvantage because we may lack the resources of some of our competitors to monitor for and detect infringement. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in any patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent’s claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly.

We may need to license or acquire additional patents and intellectual property rights.

One or more third parties may hold intellectual property rights, including patent rights, important or necessary to the development of our products. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties on commercially reasonable terms. If we were not able to obtain a license, or were not able to obtain a license on commercially reasonable terms, our business could be harmed, possibly materially.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could harm our business.

Our commercial success depends upon our ability to develop, manufacture, market and sell our products, and to use our related proprietary technologies. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products, including interference or derivation proceedings before the U.S. Patent and Trademark Office, or the USPTO. Third parties may assert infringement

claims against us based on existing patents or patents that may be granted in the future. If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue commercializing our products. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Under certain circumstances, we could be forced, including by court order, to cease commercializing our products. In addition, in any such proceeding or litigation, we could be found liable for monetary damages. Regardless of the outcome, such claims or litigation may be time-consuming and costly to defend, divert management resources and have other adverse effects on our business.

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

Our success will depend, in part, on our ability to obtain and maintain patent protection for our product candidates, preserve our trade secrets, prevent third parties from infringing upon our proprietary rights and operate without infringing upon the proprietary rights of others. Composition-of-matter patents on the biological or chemical active pharmaceutical ingredient are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection without regard to any method of use. We have filed and in-licensed composition-of-matter patent applications for all of our product candidates.

However, we cannot be certain that the claims in our patent applications to inventions covering our product candidates will be considered patentable by the USPTO and courts in the United States or by the patent offices and courts in foreign countries.

In addition to composition-of-matter patents and patent applications, we also have filed method-of-use patent applications. This type of patent protects the use of the product only for the specified method. However, this type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if these competitors do not actively promote their product for our targeted indication, physicians may prescribe these products "off-label." Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent or prosecute.

Patent applications in the United States and most other countries are confidential for a period of time until they are published, and publication of discoveries in scientific or patent literature typically lags actual discoveries by several months or more. As a result, we cannot be certain that we and the inventors of the issued patents and applications that we may in-license were the first to conceive of the inventions covered by such patents and pending patent applications or that we and those inventors were the first to file patent applications covering such inventions. Also, we have a number of issued patents and numerous patent applications pending before the USPTO and foreign patent offices and the patent protection may lapse before we manage to obtain commercial value from them, which might result in increased competition and materially affect our position in the market.

Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve technological and legal complexity, and obtaining and enforcing biopharmaceutical patents is costly, time-consuming, and inherently uncertain. The United States Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our and our licensors' or collaborators' ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the United States Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our and our licensors' or collaborators' ability to obtain new patents or to enforce existing and future patents.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our and our licensors' or collaborators' patent applications and the enforcement or defense of our or our licensors' or collaborators' issued patents. For example, the Leahy-Smith America Invents Act, or the America Invents Act, includes provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The USPTO developed new regulations and procedures to govern administration of the America Invents Act, and many of the substantive changes to patent law associated with the America Invents Act, and in particular, the first to file provisions, are now effective. While it is still not clear what, if any, impact the America Invents Act will have on the operation of our business, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors' or collaborators' patent applications and the enforcement or defense of our or our licensors' or collaborators' issued patents, all of which could have a material adverse effect on our business and financial condition.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on all of our product candidates throughout the world would be prohibitively expensive. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

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

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

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- Others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed.
- We or our licensors or strategic partners might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or have exclusively licensed.
- We or our licensors or strategic partners might not have been the first to file patent applications covering certain of our inventions.
- Others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights.
- It is possible that our pending patent applications will not lead to issued patents.
- Issued patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors.
- Our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets.
- We may not develop additional proprietary technologies that are patentable.
- The patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business, results of operations and prospects.

We may be subject to claims that we or our employees or consultants have wrongfully used or disclosed alleged trade secrets of our employees' or consultants' former employers or their clients. These claims may be costly to defend and if we do not successfully do so, we may be required to pay monetary damages and may lose valuable intellectual property rights or personnel.

Many of our employees and contractors were previously employed at universities or biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. If we fail in defending such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A loss of key research personnel or their work product could hamper our ability to commercialize, or prevent us from commercializing our product candidates, which could severely harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into invention and patent assignment agreements with our employees and consultants that obligate them to assign their inventions to us. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them from using

that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

Risks Related to Ownership of Our Common Stock

We cannot predict what the market price of our common stock will be and, as a result, it may be difficult for you to sell your shares of our common stock.

An inactive market may impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic partnerships or acquire companies or products by using our shares of common stock as consideration. We cannot predict the prices at which our common stock will trade. It is possible that in one or more future periods our results of operations may be below the expectations of public market analysts and investors and, as a result of these and other factors, the price of our common stock may fall.

The market price of our stock may be volatile, and you could lose all or part of your investment.

The trading price of our common stock is likely to be highly volatile and subject to wide fluctuations in response to various factors, some of which we cannot control. In addition to the factors discussed in this “Risk Factors” section these factors include:

- the success of competitive products or technologies;
- regulatory actions with respect to our products or our competitors’ products;
- actual or anticipated changes in our growth rate relative to our competitors;
- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures, collaborations or capital commitments;
- results of clinical trials of our product candidates or those of our competitors;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the results of our efforts to in-license or acquire additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or our other stockholders;
- changes in the structure of healthcare payment systems, including coverage and reimbursement;
- market conditions in the pharmaceutical and biotechnology sectors; and
- general economic, industry and market conditions.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

To our knowledge, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially own approximately 52% of our voting stock as of December 31, 2017. Accordingly, these stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders. The interests of this group of stockholders may not always coincide with the interests of other stockholders and they may act in a manner that advances their best interests and not necessarily those of other stockholders, including seeking a

premium value for their common stock, and might affect the prevailing market price for our common stock.

Sales of a substantial number of shares of our common stock by our existing stockholders in the public market could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. If our existing stockholders sell, or if the market perceives that our existing stockholders intend to sell, substantial amounts of our common stock in the public market, the market price of our common stock could decline significantly.

Our management will continue to have broad discretion over the use of the proceeds we received in our public offerings, private placements, warrant exercises and term loans and might not apply the proceeds in ways that increase the value of your investment.

Our management will continue to have broad discretion to use the net proceeds from our public offerings, private placements warrant exercises and term loans and you will be relying on the judgment of our management regarding the application of these proceeds. Our management might not apply our net proceeds in ways that ultimately increase the value of your investment. Because of the number and variability of factors that will determine our use of the remaining net proceeds from our initial public offering, follow-on public offering and other financing transactions, their ultimate use may vary substantially from their currently intended use. If we do not invest or apply the net proceeds from our public offerings, private placements, warrant exercises and term loans in ways that enhance stockholder value, we may fail to achieve the expected financial results, which could cause our stock price to decline.

Future sales and issuances of equity and debt securities could result in additional dilution to our stockholders and could place restrictions on our operations and assets, and such securities could have rights, preferences and privileges senior to those of our common stock.

We expect that significant additional capital will be needed in the future to fund our planned operations, including to complete clinical trials for our product candidates. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities, existing stockholders may be materially diluted by subsequent sales, and new investors could gain rights, preferences and privileges senior to the holders of our common stock.

Pursuant to our Amended and Restated 2013 Equity Incentive Plan, our management is authorized to grant up to 5,781,333 stock options or awards to our employees, directors and consultants, and the number of shares of our common stock reserved for future issuance under the plan will be subject to automatic annual increases in accordance with the terms of the plan. To the extent that new options are granted and exercised or we issue additional shares of common stock in the future, our stockholders may experience additional dilution, which could cause our stock price to fall.

We are an “emerging growth company” and we cannot be certain if the reduced disclosure requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act, or JOBS Act, and may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not “emerging growth companies” including not being required to comply with the auditor attestation requirements of section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company for up to five years following the year in which we completed our initial public offering, although circumstances could cause us to lose that status earlier, including if the market value of our common stock held by non-affiliates exceeds $700.0 million as of any June 30 before that time or if we have total annual gross revenue of $1.0 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31 or, if we issue more than $1.0 billion in non-convertible debt during any three year period before that time, we would cease to be an emerging growth company immediately. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

We incur increased costs and demands upon management as a result of being a public company.

As a public company listed in the United States, we incur significant additional legal, accounting and other costs. We are subject to the reporting requirements of the Exchange Act, which requires, among other things, that we file with the Securities and Exchange Commission, or the SEC, annual, quarterly and current reports with respect to our business and financial condition. In addition, changing laws, regulations and standards relating to corporate governance and public disclosure, including regulations implemented by the SEC and The NASDAQ Stock Market, may increase legal and financial compliance costs and make some activities more time consuming. These laws, regulations and standards are subject to varying interpretations and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. We invest resources to comply with evolving laws, regulations and standards, and this investment results in increased general and administrative expenses and a diversion of management's time and attention. If we do not comply with new laws, regulations and standards, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

Failure to comply with these rules might also make it more difficult for us to obtain some types of insurance, including director and officer liability insurance, and we might be forced to accept reduced policy limits and coverage or incur substantially higher costs to

obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, on committees of our board of directors or as members of senior management.