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# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION

**WASHINGTON, DC 20549**

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# FORM 10-K

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**(Mark One)**

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

**For the fiscal year ended December 31, 2018**

**OR**

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

**Commission File Number: 001-38080**

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## Biohaven Pharmaceutical Holding Company Ltd.

(Exact Name of Registrant as Specified in its Charter)

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| **British Virgin Islands**<br>(State or other jurisdiction of incorporation or organization) | **Not applicable**<br>(I.R.S. Employer Identification No.) |
|---|---|
| **c/o Biohaven Pharmaceuticals, Inc.**<br>**215 Church Street, New Haven, Connecticut**<br>(Address of principal executive offices) | **06510**<br>(Zip Code) |

**(203) 404-0410**
(Registrant's telephone number, including area code)

(Former address)

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

| **Title of each class** | **Name of each exchange on which registered** |
|---|---|
| Common Shares, without par value | New York Stock Exchange |

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 Section 15(d) of the Exchange 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 every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of 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 emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act. (Check one):

| Large accelerated filer ☒ | Accelerated filer ☐ | Non-accelerated filer ☐ | Smaller reporting company ☐<br>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 market value of the registrant's common shares held by non-affiliates of the registrant as of the last business day of the registrant's most recently completed second fiscal quarter, June 30, 2018, based on the last reported sale price of the registrant's common stock on the New York Stock Exchange on June 29, 2018 of $39.52, was $1.585 billion. The calculation does not reflect a determination that certain persons are affiliates of the registrant for any other purpose. As of February 26, 2019, there were 44,262,658 common shares, no par value per share, outstanding.

**Documents Incorporated by Reference**

Portions of the registrant's definitive Proxy Statement to be filed pursuant to Regulation 14A under the Securities Exchange Act of 1934 for its 2019 Annual Meeting of Shareholders are incorporated by reference into Part III of this Annual Report on Form 10-K.

**Cautionary Note Regarding Forward-Looking Statements**

This Annual Report on Form 10-K, or this report, contains forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this report are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "may", "will", "should", "expects", "intends", "plans", "anticipates", "believes", "estimates", "predicts", "potential", "continue" or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our plans to develop and commercialize our product candidates;
- our ongoing and planned clinical trials for our rimegepant, troriluzole (previously referred to as trigriluzole or BHV-4157), BHV-0223, BHV-3500, BHV-5000 and verdiperstat (previously referred to as BHV-3241) development programs;
- the timing of the availability of data from our clinical trials;
- the timing of our planned regulatory filings, including our planned NDA submissions for rimegepant;
- the timing of and our ability to obtain and maintain regulatory approvals for our product candidates;
- the clinical utility of our product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position; and
- our estimates regarding future revenues, expenses and needs for additional financing.

Any forward-looking statements in this report reflect our current views with respect to future events and with respect to our future financial performance and 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, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those described under Part I, Item 1A. Risk Factors and elsewhere in this report. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward- looking statements for any reason, even if new information becomes available in the future.

This report contains estimates, projections and other information concerning our industry, the general business environment, and the markets for certain diseases, including estimates regarding the potential size of those markets and the estimated incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events, circumstances or numbers, including actual disease prevalence rates and market size, may differ materially from the information reflected in this report. Unless otherwise expressly stated, we obtained this industry, business information, market data, prevalence information and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data, and similar sources, in some cases applying our own assumptions and analysis that may, in the future, not prove to have been accurate.

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**PART I**

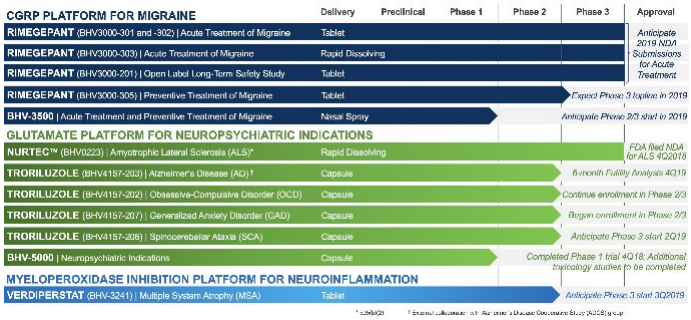
**Item 1. Business**

**Overview**

We are a clinical-stage biopharmaceutical company with a portfolio of innovative, late-stage product candidates targeting central nervous system diseases, including neurological and rare disorders. Most of our product candidates are small molecules and based on three distinct mechanistic platforms—calcitonin gene-related peptide ("CGRP") receptor antagonists, glutamate modulators, and myeloperoxidase inhibitor—which we believe have the potential to significantly alter existing treatment approaches across a diverse set of indications with high unmet need in both large and orphan indications.

**Product Candidates**

The following table summarizes our most advanced development programs. We hold the worldwide rights to all of our product candidates.




**Our CGRP Receptor Antagonist Platform**

*Migraine Overview and Market Opportunity*

Migraine is a chronic and debilitating disorder characterized by recurrent attacks lasting four to 72 hours with multiple symptoms, including typically one-sided, pulsating headaches of moderate to severe pain intensity that are associated with nausea or vomiting, and/or sensitivity to sound (phonophobia) and sensitivity to light (photophobia). Migraines are often preceded by transient neurological warning symptoms, known as auras, which typically involve visual disturbances such as flashing lights, but may also involve numbness or tingling in parts of the body. Migraine is both widespread and disabling. The Migraine Research Foundation ranks migraine as the world's third most prevalent illness, and the Global Burden of Disease Study 2015 rates migraine as the seventh highest specific cause of disability worldwide. According to the Migraine Research Foundation, in the United States, approximately 36 million individuals suffer from migraine attacks. While most sufferers experience migraine attacks once or twice per month, more than 4 million people have chronic migraine, defined as experiencing at least 15 headache days per month, of which at least eight are migraine, for more than three months. Others have episodic migraine, which is characterized by experiencing less than 15 migraine days per month. People with frequent episodes of migraine may progress to chronic migraine over time. Migraine attacks can last four hours or up to three days. More than 90% of individuals suffering from migraine attacks are unable to work or function normally during a migraine attack, with many experiencing comorbid conditions such as depression, anxiety and insomnia.

Triptans are the current first-line prescription therapy for the acute treatment of migraine, with over 13.9 million annual prescriptions in the United States. Despite the market for triptans being highly genericized, branded options continue to be popular. For example, even at a price of approximately $400-600/month, Maxalt is a commonly prescribed triptan. There has been minimal improvement in the standard treatment for migraine since the early 1990s. Reformulations of generic triptans or incremental improvements with new agents that target the same pathway are predicted to generate additional sales in the near

term, but major sales growth for the migraine market are expected from novel therapeutics over the next several years. We believe that rimegepant will be a potential best-in-class small molecule CGRP receptor antagonist for the acute treatment of migraine and could achieve meaningful penetration of the market of migraine sufferers whose symptoms are not adequately addressed with current treatments. It is important to recognize that all migraine patients require acute treatment, including patients who take preventive medicine (as they typically do not eliminate all migraine attacks).

The prevention of migraine in the United States is a multi-billion dollar potential market. According to a report published by *Neuropsychiatric Disease and Treatment*, 38% to 50% of diagnosed migraine sufferers may be candidates for migraine prevention therapy. Currently, preventive medications approved for migraine include beta blockers, such as propranolol, topiramate, sodium valproate, and botulinum toxin ("Botox") (chronic migraine only) and generate nearly 10 million prescriptions annually. Three CGRP monoclonal antibodies (mABs) were approved in 2018 for the preventive treatment of migraine in adults. There was rapid early uptake of this class, but utilization will be defined over the next 24 months.

In patients with high frequency and chronic migraine, beta blockers, topiramate and sodium valproate are commonly used to reduce the frequency of migraine. These medications are often not well tolerated by patients because of adverse events ("AEs") such as cognitive impairment, nausea, fatigue and sleep disturbance. In clinical trials with topiramate, the reduction in number of migraine days per month has been observed to be relatively small; for example, migraine days reduced by 2.5 days from six to seven days at baseline, or reduced by 3.5 days from 15 to 16 days at baseline. Migraine is twice as prevalent in women as compared to men. In the affected female patient population, predominantly women of child-bearing age, the association of these agents with poor pregnancy outcomes and fetal abnormalities can limit their use. Botox is only approved for the prevention of migraine in patients diagnosed with chronic migraine. Approximately 47% of Botox-treated patients experience a 50% reduction in either migraine days per month or migraine frequency per month within six months, which leaves more than half of patients inadequately treated. In addition, the Botox dosing regimen consists of approximately 31 subcutaneous injections at various sites on the head and neck, with recommended repetition every 12 weeks if the patient has a therapeutic response.

The CGRP mAbs have a similar profile across the agents approved to date. The three new FDA-approved drugs, Aimovig (erenumab-aooe), Ajovy (fremanezumab-vfrm), and Emgality (galcanezumab-gnlm), are all administered subcutaneously. The side effects from the new CGRP monoclonal antibody drugs are generally mild, including pain and redness at the site of injection and nasal congestion. Studies show that the monoclonal antibodies reduce the number of headache days by 50% or more in approximately half of the patients who take them. In only a small percentage of patients do these drugs eliminate migraine attacks, with the vast majority of patients also needing additional effective acute treatment.

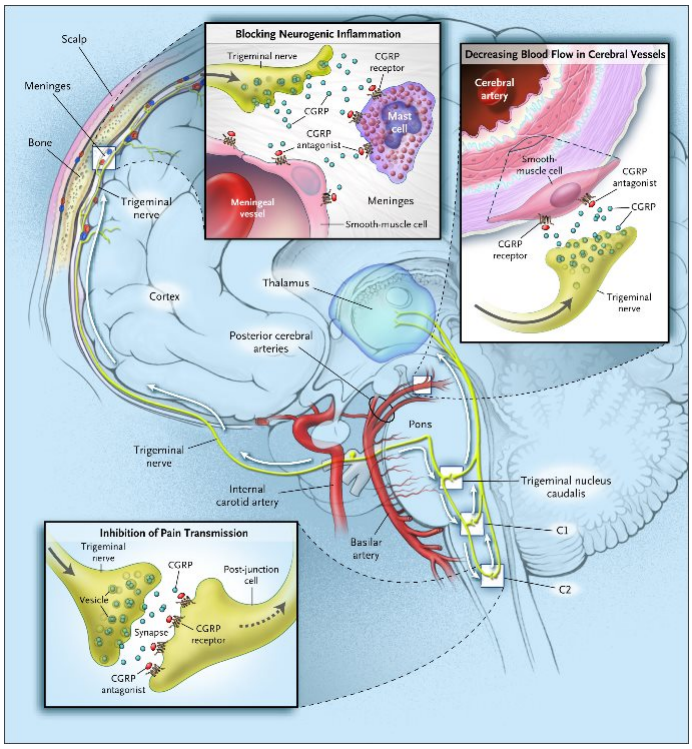
*CGRP's Role in Migraine*

The CGRP receptor is located within pain-signaling pathways, intracranial arteries and mast cells and its activation is thought to play a causal role in migraine pathophysiology. For example, research and clinical studies have shown serum levels of CGRP are elevated during migraine attacks, infusion of intravenous CGRP produces persistent pain in migraine sufferers and non-migraine sufferers, and treatment with anti-migraine drugs normalizes CGRP activity. Additionally, multiple clinical studies show that small molecule CGRP receptor antagonists, which inhibit the binding of endogenous CGRP to CGRP receptors, are effective in the acute treatment of migraine attacks.

Treatment with a CGRP receptor antagonist is believed to relieve migraine through the following mechanisms:

- **Blocking Neurogenic Inflammation:** Binding of CGRP receptor antagonists to CGRP receptors located on mast cells inhibits inflammation caused by trigeminal nerve release of CGRP onto mast cells within the tough outer covering of the brain, or the meninges.
- **Decreasing Artery Dilation:** By blocking the CGRP receptors located in smooth muscle cells within vessel walls, CGRP receptor antagonists inhibit the pathologic dilation of intracranial arteries without the unwanted effect of active vasoconstriction.
- **Inhibiting Pain Transmission:** Binding of CGRP receptor antagonists to CGRP receptors suppress the transmission of pain by inhibiting the central relay of exaggerated pain signals from the trigeminal nerve to the caudal trigeminal nucleus.

The graphic below depicts the mechanism of action by which CGRP receptor antagonism is thought to alleviate migraine.

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From N Engl J Med, Durham PL, CGRP-Receptor Antagonists — A Fresh Approach to Migraine Therapy? 350:1073-1075, Copyright © 2018 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

***Our Lead Product Candidate: Rimegepant, an Oral CGRP Receptor Antagonist for the Acute and Preventive Treatment of Migraine***

We are developing rimegepant as an orally available, selective and potent small molecule CGRP receptor antagonist for the acute and preventive treatment of migraine. The first indication being pursued is the acute treatment of migraine. We believe

that rimegepant has the potential to be the best-in-class CGRP receptor antagonist for the acute treatment of migraine with the ability to address important unmet needs, such as early onset of pain relief, durable efficacy of pain relief and relief from most bothersome symptoms and rapid return to normal function (decreased disability). Importantly, these benefits are noted without the cardiovascular contraindications of triptan therapy and/or the bothersome side effects that impact utilization. Additionally, oral small molecule CGRP receptor antagonists with high receptor affinity and long half-lives, such as rimegepant, may possess dual-therapy action with ability to provide both acute relief and preventive effects.

In July 2017, we initiated two Phase 3 clinical trials of rimegepant, and we completed enrollment in these trials in November 2017. Topline results from both of these Phase 3 trials were reported in March, 2018. The co-primary endpoints (pain freedom at 2 hours and reduction of most bothersome symptoms) were both met as well as key secondary endpoints (return to function, pain relief). These results are described in greater detail below under "—Our Clinical Program for Rimegepant in Acute Treatment of Migraine— Phase 3 Clinical Trials: Studies 301 and 302."

Those suffering from migraine often have accompanying nausea and have an aversion to consuming food or liquids during an attack. We are also developing an oral solid dosage formulation of rimegepant that disperses almost instantly in the mouth, without the need for water. The Zydis oral dissolving tablet ("ODT") formulation being utilized uniquely addresses this issue. We have exclusive worldwide rights to the Zydis ODT fast-dissolving formulation for the development of rimegepant pursuant to a January 2018 license agreement with Catalent U.K. Swindon Zydis Limited, a subsidiary of Catalent, Inc. ("Catalent"). The agreement also provides exclusivity with respect to other small molecule CGRP receptor antagonists with the Zydis ODT technology. In February 2018, a bioequivalence study was conducted to compare this new ODT formulation to the tablet in current clinical development and provided evidence of equivalence. A third Phase 3 clinical trial evaluatiing the Zydis ODT formulation of rimegepant commenced in February 2018 and the results from this trial were reported in December 2018.

Consistent with the prior Phase 3 studies, the ODT formulation met the co-primary endpoints of pain freedom and freedom from the most bothersome symptoms. Importantly the Zydis ODT formulation had a faster onset of action with rapid onset of pain relief beginning to show an effect as early as 15 minutes and becoming statistically significant by 60 minutes. Furthermore, this study met 21 consecutive pre-specified, hierarchically tested outcome measures including durability of effect out to 48 hours post-dose without the use of rescue medication. Importantly, consistent with the other trials, placebo-level tolerability was also noted. These results are described in greater detail below under "—Our Clinical Program for Rimegepant in Acute Treatment of Migraine— Phase 3 Clinical Trials: Study 303."

In December 2018 data became available from our ongoing rimegepant long-term safety study. The positive results from the interim analysis of this trial included over 91,000 doses of rimegepant 75 mg across 1,780 patients with migraine. The safety and tolerability profile of rimegepant with up to one year of dosing in patients with migraine was consistent with the safe and well tolerated profile previous seen in clinical trials with rimegepant. No liver safety signal was detected, including a subset of patients with near-daily dosing (≥15 doses/month). Additionally, preliminary efficacy observations suggest that intermittent dosing of rimegepant 75 mg may reduce the number of headache days per month and a separate, double-blind placebo controlled preventive treatment study with rimegepant is being conducted. Overall, safety and tolerability data from this interim analysis and ongoing data from this study are expected be sufficient to support new drug application ("NDA") submissions for the Zydis ODT and tablet formulations planned for second quarter of 2019.

Based on emerging data from repeat dosing of rimegepant in the long-term safety trial, a Phase 3 trial to evaluate rimegepant as a preventative treatment of migraine was initiated in November 2018.

In November 2017, we received agreement from the FDA on an initial pediatric study plan. In 2018, we submitted requests for scientific advice for rimegepant to the Committee for Medicinal Products for Human Use ("CHMP") a committee of the European Medicines Agency ("EMA") and feedback suggests there are several options for pursuing indications for rimegepant in Europe which are currently under consideration.

Additionally, in January 2019, we announced with our wholly-owned subsidiary, BioShin, that the National Medical Products Administration (formerly, the China FDA) has accepted the investigation new drug ("IND") application for rimegepant for the treatment of migraine. We had previously announced the formation of BioShin in November of 2018; the subsidiary was established to develop and potentially commercialize our late-stage migraine and neurological disorder product development portfolio in China and other Asia-Pacific markets.

*Acute Treatment of Migraine and Limitation of Current Treatments*

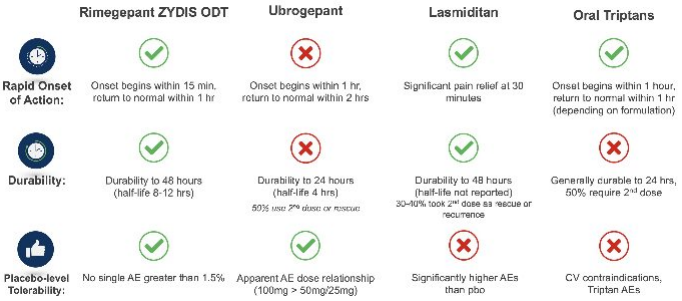
Clinicians use a number of pharmacologic agents for the acute treatment of migraine. A study published by the American Headache Society in 2015 concluded that the medications deemed effective for the acute treatment of migraine fell into the following classes: triptans, ergotamine derivatives, non-steroidal anti-inflammatory drugs ("NSAIDs"), opioids and combination medications. The current standard of care for the acute treatment of migraine is prescription of triptans, which are serotonin 5-HT$_{1B/1D}$ receptor agonists. Triptans have been developed and approved for the acute treatment of migraine over the

past two decades. The initial introduction of triptans represented a shift toward drugs more selectively targeting the suspected pathophysiology of migraine. While triptans account for almost 80% of anti-migraine therapies prescribed at office visits by healthcare providers, issues such as an incomplete effect or headache recurrence remain important clinical limitations. In fact, for any given attack, almost 50% of patients take a second dose in search of pain relief. In addition, triptans are contraindicated in patients with cardiovascular disease, cerebrovascular disease, or significant risk factors for either because of potential systemic and cerebrovascular vasoconstriction from the 5-HT1B-mediated effects. The package insert for triptans includes warnings and precautions for migraine patients with risk factors for cardiovascular disease and states that high risk patients, including those with increased age, diabetes, hypertension, smoking, obesity or a strong family history of coronary artery disease, should be evaluated prior to receiving the first dose of a triptan. Triptans are contraindicated in patients with a history of ischemic heart disease, coronary artery vasospasm, history of stroke, peripheral vascular disease or uncontrolled hypertension. Even in patients who have a negative cardiovascular evaluation, product labeling for triptans recommends that consideration be given to administration of the first dose in a medically-supervised setting and performing an electrocardiogram immediately following administration. Additionally, periodic cardiovascular evaluation should be considered for long-term users of triptans who have cardiovascular risk factors. According to a January 2017 study published in the journal *Headache*, an estimated 2.6 million migraine sufferers in the United States have a cardiovascular event, condition or procedure that limits the potential of triptans as a treatment option. Thus, we believe there remains a significant unmet medical need for a novel migraine-specific medication that does not increase the risk of cardiovascular liability.

*The Potential Benefits of Rimegepant Compared to Other Treatments*

Traditionally, for approval of drugs for the acute treatment of migraine, the FDA required the drug to meet four co-primary endpoints at two hours after dosage in clinical trials: pain freedom or pain relief, and freedom from nausea, phonophobia and photophobia. In October 2014, the FDA issued new guidance (and formal guidance in February 2018) indicating that pivotal migraine trials could use a preferred approach of co-primary 2-hour endpoints of freedom from pain and freedom from most bothersome symptom (among nausea, photophobia or phonophobia) to support approval.

The table below compares what we believe are key features of rimegepant contrasted to other product candidates and standard of care treatments for the acute treatment of migraine.*




*These are cross-trial comparisons and no comparative head-to-head studies between rimegepant and competitors have been conducted.

Based on the results from the rimegepant clinical trials to date, we believe rimegepant offers the following clinical and product benefits for the acute treatment of migraine:

- **Oral Availability.** Rimegepant is the only oral CGRP currently formulated in a Zydis ODT that can be administered sublingually for the potential for rapid onset of action. In our Phase 3 clinical trial, the rimegepant Zydis ODT formulation demonstrated pain relief beginning as early as 15 minutes (becoming statistically significant by 60 minutes), with patients returning to normal functioning by 60 minutes. We have an exclusive worldwide agreement with Catalent for the use of rimegepant in the Zydis ODT fast-dissolving formulation (which also provides exclusivity with respect to other small molecule CGRP receptor antagonists with the Zydis ODT technology). We believe oral availability in an easy to use formulation will provide advantages over injectable migraine treatments.
- **Comprehensive Treatment Effect.** Rimegepant has demonstrated consistent comprehensive treatment effect across 3 large Phase 3 trials and a Phase 2b trial with significant pain freedom, pain relief and relief from most bothersome symptoms. These effects were all noted with a single dose of the 75 mg tablet or ODT. The majority of patients treated with a single dose of rimegepant 75 mg did not require the use of additional rescue medications after treating their migraine.
- **Durable Improvement.** In the Phase 3 trials, rimegepant demonstrated durable impact on pain freedom and pain relief through 48 hours compared to placebo. We believe that this durability of effect is related to the half-life of rimegepant and is an important differentiator from other products that have a shorter half-life and require additional doses of medications or rescue medications.
- **Favorable Safety Profile.** In 3 Phase three studies of over 3500 patients, rimegepant demonstrated a safety profile similar to placebo. There were no AEs greater than 1.6%. Consistent with the preclinical data, there was no clinical evidence suggesting that rimegepant has vasoconstrictor activity or other undesirable cardiovascular side effects, such as changes in the blood pressure or heart rate, that are commonly associated with triptans.
- **Potency.** Rimegepant is highly potent with subnanomolar affinity for the human CGRP receptor, which allows for a relatively low dose to provide maximal treatment effect with a single 75 mg dose.
- **Lower Expected Cost.** We expect that as a small molecule, rimegepant will have a lower cost of goods than CGRP antibodies, which are biologics.

*The Potential of CGRP Antagonists: Novel mechanism of action without causing vasoconstriction*

The release of the neuropeptide CGRP from pain nerves is believed to play a causal role in the underlying pathophysiology of migraine and is also a potent dilator of intracranial arteries. Unlike triptans, which possess potent vasoconstrictive properties that could worsen cardiovascular or cerebrovascular disease, blocking the CGRP receptor reverses pathologic dilation of blood vessels without constricting them past their normal resting state size and without active vasoconstriction. The absence of cardiovascular effects may prove to be one of the major advantages in the use of CGRP receptor antagonists for the treatment of migraine. Preclinical and clinical evidence suggests that the use of CGRP receptor antagonists may be effective in treating migraine by blocking the pathophysiological processes associated with CGRP release, specifically by: (1) inhibiting pain transmission; (2) decreasing artery dilation without any active vasoconstriction; and (3) halting neurogenic inflammation. To date, the preclinical and clinical evidence indicates that CGRP receptor antagonists have an absence of vasoconstrictor activity and lack other undesirable cardiovascular side effects, such as changes in the blood pressure or heart rate. Studies of numerous drugs in development have provided proof of concept of the effects of CGRP targeting agents in humans.

*Our Clinical Program for Rimegepant in Acute Treatment of Migraine*

We licensed rimegepant from BMS in July 2016. BMS selected rimegepant as a lead CGRP receptor antagonist compound for its potential best-in-class chemical profile after 10 years of research on this drug target.

*Phase 3 Clinical Trials: Studies 301 and 302*

Based on favorable results observed in a Phase 2b clinical trial, we elected to advance the 75 mg dose of rimegepant in our Phase 3 clinical trials. According to FDA 2014 draft guidance for developing drugs for acute treatment of migraine, approval for this indication has historically involved the demonstration of an effect on four co-primary endpoints: pain, nausea, photophobia and phonophobia. More recently, the agency has considered an alternate approach and in the recently published FDA 2018 formal guidance indicated as the "preferred approach" for approval based on an effect at 2 hours on headache pain freedom and freedom from a patient's most bothersome migraine symptom, or MBS, selected as either nausea, photophobia or phonophobia. Using this approach, the two co-primary endpoints would be (1) having no headache pain at two hours after dosing and (2) a demonstrated effect on freedom from the MBS at two hours after dosing. Regardless of the associated symptom identified as most bothersome, the FDA guidance states that all three important migraine symptoms (nausea, photophobia and phonophobia) should be assessed as secondary endpoints.

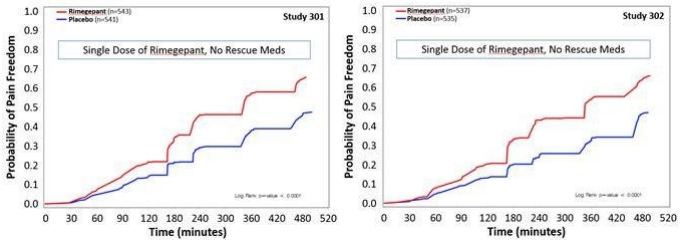
We held an end of Phase 2 meeting with the FDA in March 2017 and commenced two Phase 3 clinical trials ("Study 301" and "Study 302") in July 2017 with the oral tablet. We completed enrollment in these trials in November 2017. Approximately 3,000 patients were enrolled and 2,300 patients randomized across these two Phase 3 trials.

We believe that our Phase 3 trials of rimegepant 75 mg conform to the FDA guidance for approval in acute treatment of migraine. The trials were double-blinded, randomized, and placebo-controlled. The first two Phase 3 trials treated subjects with the tablet version of rimegepant and recruited male and female patients 18-65 years of age with at least a one year history of migraine, including an age of onset prior to 50, migraine attacks that last about four to 72 hours, not more than eight attacks of moderate to severe intensity per month within the last three months and not less than two attacks per month. Our goal was to enroll patients who represent the spectrum of real-world migraine patients, including those who have previously been non-responsive to triptans, as the FDA stated to us at our end of Phase 2 meeting that triptan-resistant patients may benefit from rimegepant treatment. We also enrolled patients who had cardiovascular risk factors and/or vascular disease. The primary objective of the trials was to evaluate the efficacy of 75 mg of rimegepant compared with placebo in the acute treatment of migraine as measured by two co-primary endpoints: (1) pain freedom (headache pain intensity level reported as "no pain") at two hours after dosing using a four-point numeric rating scale (no pain, mild pain, moderate pain, severe pain) and (2) freedom from the MBS at two hours after dosing. The three other important migraine symptoms (nausea, photophobia and phonophobia) were assessed as secondary endpoints, consistent with FDA guidance.

In March 2018, we announced positive topline data from our first two Phase 3 clinical trials of rimegepant. In each trial, treatment with a single 75 mg dose of rimegepant met the co-primary efficacy endpoints of the trial, which were superior to placebo, at two hours post-dose, on measures of pain freedom and freedom from the patient's most bothersome symptom, or MBS, selected as either nausea, photophobia or phonophobia.

The figures below show, for each trial, Kaplan-Meier curves depicting the effect of rimegepant on pain freedom as compared to placebo over the course of eight hours after dosing. A Kaplan-Meier curve is a method of statistical analysis used to show estimates of data over time even though data was only collected at intervals throughout that time period.

**Kaplan-Meier Curve Showing Pain Freedom 0-8 Hours Post-Dosing**




Rimegepant showed a numerical improvement in pain freedom as compared to placebo as early as 45-60 minutes post-dosing, with continued improvement over the course of eight hours post-dosing. The magnitude of the treatment effect over placebo at two hours post-dosing or later, as shown in the figures above, ranged from 5% to 19% in Study 301 and 7% to 22% in Study 302. This continued improvement in pain freedom was observed in patients who received a single dose of rimegepant and did not use rescue medications. Rescue medications are additional medications that patients in clinical trials may take concurrently with the study drug or placebo after the 2 hour endpoint has been registered when the patient experiences inadequate relief. Each of the figures above excludes patients who took rescue medication or who were lost to follow-up during the specified interval.

Pain freedom at two hours post-dosing, one of the co-primary endpoints of these trials, was 19.2% and 19.6% for rimegepant-treated patients in Study 301 and 302, respectively, as compared to 14.2% and 12.0% for patients receiving placebo, with corresponding p-values of <0.03 and <0.001, respectively. P-value is a conventional statistical method for measuring the

statistical significance of clinical results. A p-value of 0.05 or less represents statistical significance, meaning that there is a less than 1-in-20 likelihood that the observed results occurred by chance. The table below summarizes these results.

Rimegepant also achieved statistically significant results on a second co-primary endpoint, freedom from MBS, selected from photophobia, phonophobia or nausea, at two hours post-dosing. As shown in the table below, freedom from MBS for patients treated with rimegepant were 36.6% and 37.6% in Study 301 and Study 302, respectively, as compared to 27.7% and 25.2% for patients receiving placebo, with corresponding p-values of <0.002 and <0.0001, respectively.

**Co-Primary Regulatory Endpoints in Study 301 and 302**

**Study 302**

| **2 Hour Endpoint** | **Rimegepant** (N=537) | | **Placebo** (N=535) | | **p-value** |
|---|---|---|---|---|---|
| Pain Freedom | 19.6 | % | 12.0 | % | < 0.001 |
| Freedom from MBS[1] | 37.6 | % | 25.2 | % | < 0.0001 |

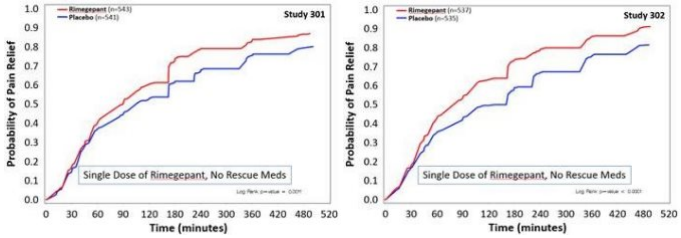
**Study 301**

| **2 Hour Endpoint** | **Rimegepant** (N=543) | | **Placebo** (N=541) | | **p-value** |
|---|---|---|---|---|---|
| Pain Freedom | 19.2 | % | 14.2 | % | < 0.03 |
| Freedom from MBS[1] | 36.6 | % | 27.7 | % | < 0.002 |

(1) MBS: Most Bothersome Symptom of Photophobia, Phonophobia or Nausea.

We also evaluated rimegepant' s effect on pain relief, which is the transition from experiencing moderate-to-severe pain to either no pain or mild pain, as a secondary endpoint in both trials. Although pain relief does not always indicate that a patient has no pain, unlike pain freedom, it is a clinically important endpoint because it often is associated with reduced disability due to migraine attacks. In each of the Phase 3 trials, onset of pain relief in patients treated with rimegepant was observed early after dosing, with separation between rimegepant and placebo evident between 30 and 45 minutes post-dosing. In both trials, by two hours post-dosing, over 55% of patients receiving only a single dose of rimegepant achieved pain relief (p-values of 0.0006 in Study 301 and <0.0001 in Study 302). The figures below show, for each trial, Kaplan-Meier curves depicting the effect of rimegepant on pain relief as compared to placebo over the course of eight hours after dosing.

**Kaplan-Meier Curve Showing of Time to Pain Relief Up to 8 Hours Post Single Dose**




Each of the figures above excludes patients who took rescue medication or who were lost to follow-up during the specified interval.

In addition to achieving both co-primary endpoints in each of the trials, rimegepant also was observed to be generally well-tolerated in the trials, with a safety profile similar to placebo. In particular, pooled liver function test, or LFT, results showed that rimegepant was no more likely than placebo to increase ALT or AST levels above the upper limit of normal, or ULN. An LFT is a blood test that gives an indication of whether the liver is functioning properly. Across both trials, one patient treated with placebo and one patient treated with rimegepant showed LFTs above 3x ULN.

In both trials, no single adverse event, or AE, occurred with an incidence higher than 2% and the overall AE rates in the rimegepant groups were similar to those in the placebo groups. The most common AEs seen in patients treated with rimegepant were similar to placebo in a pooled analysis of both trials. There were no serious adverse events, or SAEs, determined by the study investigators to be drug related.

*Phase 3 Clinical Trials: Study 303*

Our third Phase 3 trial was a randomized, controlled Phase 3 clinical trial ("Study 303") evaluating the efficacy and safety of rimegepant 75 mg Zydis ODT conducted with the rimegepant 75 mg Zydis ODT and was initiated after bioequivalence between the tablet and ODT were established. This Phase 3 Zydis ODT sStudy 303 was conducted to further characterize the ODT formulation and was designed in keeping with the previous Phase 3 studies.

In December 2018, we announced positive topline data from Study 303. In Study 303, rimegepant Zydis ODT statistically differentiated from placebo on the two co-primary endpoints as well as the first 21 consecutive primary and secondary outcome measures that were pre-specified in hierarchical testing. Consistent with the two previous Phase 3 clinical trials, Study 303 met its co-primary endpoints of pain freedom and freedom from most bothersome symptom (MBS) at 2 hours using a single dose (Table 1). Importantly, patients treated with the rimegepant Zydis ODT formulation began to numerically separate from placebo on pain relief as early as 15 minutes, and this difference was statistically significant at 60 minutes ($p < 0.0001$) (Figure 1). Additionally, a significantly greater percentage of patients treated with rimegepant Zydis ODT returned to normal functioning by 60 minutes as compared to placebo ($p < 0.002$). Lasting clinical benefit was observed through 48 hours after a single dose of rimegepant on freedom from pain ($p < 0.001$), pain relief ($p < 0.001$), freedom from the most bothersome symptom ($p < 0.001$), and freedom from functional disability ($p < 0.003$). Superiority over placebo was also demonstrated in multiple other secondary endpoints. The vast majority of rimegepant Zydis ODT treated patients (85%) did not use any rescue medications.

**Table 1: Met Co-Primary Endpoints of Pain Freedom & Freedom from Most Bothersome Symptom**

| **2 Hour Endpoint** | **Rimegepant** (N=669) | | **Placebo** (N=682) | | **Difference** | | **p-value** |
|---|---|---|---|---|---|---|---|
| Pain Freedom | 21 | % | 11 | % | 10 | % | < 0.0001 |
| Freedom from MBS(1) | 35 | % | 27 | % | 8 | % | 0.0009 |

(1) Most Bothersome Symptom of Photophobia, Phonophobia or Nausea

**Figure 1: Kaplan-Meier Pain Relief Curve Through 2 Hours after Single Dose of Rimegepant 75 Mg Zydis ODT**

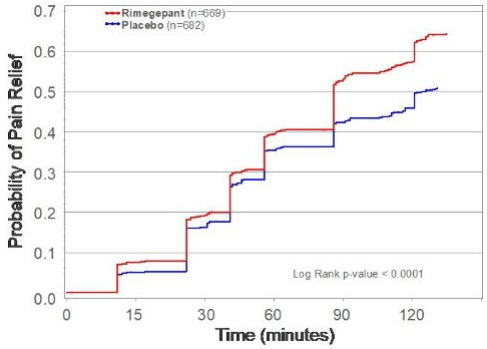



Figure 1 shows the percentage of patients reporting pain relief between 0 and 2 hours after dosing for patients who took a single dose of rimegepant Zydis ODT 75 mg or placebo. Data are Kaplan-Meier estimates of the time to first report of pain relief (report of no pain, or mild pain). Subjects were censored who took rescue medication or were lost to follow-up.

The safety and tolerability observations of rimegepant in Study 303 were consistent with the profile previously observed in Studies 301 and 302. Table 2 shows the pooled safety data across all three trials. In study 303, no single adverse event (AE) occurred in the rimegepant group with an incidence higher than 1.6% and overall rates of AEs were similar to placebo. With regard to liver function tests, one patient treated with placebo and one patient treated with rimegepant showed LFTs > 3x ULN in Study 303. Pooled liver function test results across the three pivotal trials (n=3,556) performed to date showed that rimegepant was similar to placebo with regard to aminotransferase (ALT or AST) levels above the upper limit of normal (ULN) and no patients experienced elevations in bilirubin > 2x ULN (Table 3).

**Table 2: Pooled AE Safety Data: Rimegepant was Similar to Placebo Across Studies**

**AEs from Studies 301, 302 and 303 with an incidence ≥ 1%**

| **Adverse Event** | **Rimegepant** N=1,771 | **Placebo** N=1,785 |
|---|---|---|
| ≥ 1 On-Study AE[1] | 252 (14.2)% | 209 (13.2)% |
| Nausea | 26 (1.5)% | 15 (0.8)% |
| UTI | 21 (1.2)% | 12 (0.7)% |
| SAEs[2] | 3 (0.2)% | 3 (0.2)% |

(1) No other individual AEs ≥ 1% in rimegepant treated subjects than those listed in table. Includes all AEs without attribution to drug relatedness.
(2) No drug-related Serious Adverse Events (SAEs). Two of the subjects with SAE in rimegepant group and one in placebo group had not been dosed before onset of SAE.

**Table 3: Pooled Liver Function Test (LFT) Profile: Rimegepant was Similar to Placebo Across Studies**

**Pooled LFT Results from Studies 301, 302, and 303***

| ALT or AST | Rimegepant N=1,771 | Placebo N=1,785 |
|---|---|---|
| > ULN(1) | 48 (2.7%) | 52 (2.9%) |
| > 3x ULN | 2 (0.1%) | 2 (0.1%) |
| > 5x ULN | 1 (0.06%)(2) | 0 |
| > 10x ULN | 0 | 0 |
| > 20x ULN | 0 | 0 |

(1) Upper limit of normal; ALT alanine aminotransferase; AST aspartate aminotransferase
(2) AST elevation, Not Drug-Related as deemed by the investigator: subject newly initiated weight-lifting with laboratory results consistent with muscle injury
* AST/ALT Categories are not mutually exclusive; No bilirubin elevations > 2x ULN across Studies 301, 302 and 303

*Phase 3 Clinical Trials: Long-term Safety Study (Study 201)*

In August 2017, we commenced a long-term safety study ("Study 201") to meet FDA requirements for approval. This study is a 12-month, long-term, open label safety study conducted in patients with migraine. Approximately 2,000 patients will be treated in this study. A subset of approximately 600 patients will have a history of more frequent migraine attacks (i.e., more than eight migraine attacks per month) and will be able to take up to 30 doses of 75 mg rimegepant in one month. At our end of Phase 2 meeting, the FDA stated its desire to see a safety study in which patients received daily or near-daily dosing of rimegepant for at least three months. This desire stems from the FDA's concern about a potential liver signal with the class of CGRP antagonists. The FDA stated that any risk of liver injury has to be very low and that exposure with the drug has to be sufficient to cap the risk of liver injury at a level acceptable for the migraine population. We believe the design of our long-term safety study may adequately address this concern by providing for the enrollment of approximately 600 patients who experience nine to fourteen migraine episodes per month and will be allowed to use rimegepant on a daily basis, which we believe will generate safety data with respect to long-term, frequent use of rimegepant. Importantly, we believe this study design, where patients are allowed to take up to 30 doses of 75 mg rimegepant in one month, embraces the FDA guidance for conduct of a long-term safety trial during which patients can treat all acute migraine episodes with the investigational drug. Study visits for all patients are monthly for the first three months and every three months thereafter. Based on feedback we received at our end of Phase 2 meeting with the FDA, we are administering liver function testing at two weeks post-dose and will follow patients with any abnormal liver function tests until clinical resolution.

On December 10, 2018, we announced initial positive results from the ongoing safety study. As of November 21, 2018 (the database cutoff date of the interim assessment), Over 91,000 doses of rimegepant 75mg had been administered across 1,780 patients with migraine, and approximately 473 of those patients had received near daily dosing (15 or more doses a month) of rimegepant 75 mg for a duration of 1-12 months. Based on this interim analysis, it appears that rimegepant may be safe and well tolerated with long-term dosing in patients with migraine.

The interim results also include hepatic safety and tolerability data of rimegepant 75 mg in study participants based upon review of both adverse events and regularly scheduled liver function tests. Interim hepatic data were reviewed by an external independent panel of liver experts. The panel provided a consensus opinion based upon the Drug-Induced Liver Injury Network (DILIN) causality assessment. The panel did not assess any liver cases as probably related to study drug and there were no Hy's Law cases identified. The panel concluded that there was no liver safety signal detected through the data analysis cut-off date, including in a subset of patients with near-daily dosing (> 15 doses/month). In aggregate, the panel noted that, compared to placebo arms of other migraine treatments, there was a very low incidence of overall elevations of liver laboratory abnormalities (1.0% incidence of serum ALT or AST > 3xULN). Subjects will continue to participate in Study 201 with additional data analyses to be submitted to the FDA in connection with the planned NDA submissions, including the required 120-day safety update.

The most common individual AEs (occurring > 5%) in Study 201 were upper respiratory tract infection and viral respiratory tract infection. There were low rates of discontinuation due to AEs in the treatment period (2.6%).

In addition to the interim safety analysis, preliminary open-label efficacy data from Study 201 suggest that rimegepant may be associated with a reduction in migraine days per month (30 days) compared to the observational lead-in period, suggesting a potential preventive effect. In an exploratory analysis, patients who experienced > 15 migraine days/month (N=172) during the standard of care observation period demonstrated a mean reduction of 4 headache days/month by 12 weeks

of intermittent dosing with rimegepant. Reduction from baseline in the mean number of headache days per month was observed beginning as early as the first month and continued in subsequent months of therapy.

In addition to Study 201, clinical monitoring for potential hepatotoxicity has been and will continue to be conducted in subsequent studies in humans. Such monitoring will include routine liver function tests including ALT, AST, total bilirubin, GGT and ALP at all study phases, including screening (before exposure to rimegepant), regularly during exposure, and after exposure. Additionally, the frequency, severity, and discontinuations of hepatic-related AEs are monitored closely. All cases of DILI are reported as SAEs. Other symptoms or target organs from nonclinical studies that will continue to be followed include skeletal muscle effects, emesis, skin rash and hematology measures. The two-year carcinogenicity study completed in the fourth quarter of 2018 and we expect to receive the study report in 2019.

*Our Clinical Program for Rimegepant in Preventative Treatment of Migraine*

A Phase 3 clinical trial in the preventive treatment of migraine was initiated in November of 2018 to examine the efficacy and safety of rimegepant 75 mg dosed on an intermittent schedule planned for 800 adult subjects who have suffered from migraine for at least one year and who have a frequency of 4 to 14 migraine attacks of moderate to severe pain intensity per month over the three months prior to enrollment. The primary outcome measure is the change from baseline at week 12 in the mean number of migraine days per month. Secondary outcome measures include the achievement of at least a 50% reduction from baseline in mean monthly migraine days across the double-blind treatment phase, and the mean number of rescue medication days per month, each as measured over the course of the double-blind, treatment phase. We expect to report topline results from this trial in 2019.

*Clinical Trials with Rimegepant*

As of February 2019, nineteen clinical trials have been completed (enrollment and treatment completed) in healthy volunteers and patients with migraine that inform pharmacokinetic, metabolic interactions, safety, tolerability and efficacy of rimegepant. Rimegepant has been observed to be generally well tolerated in humans when given as single oral doses up to the maximum dose of 1500 mg and multiple oral doses up to the maximum daily dose of 600 mg for 14 days. No deaths have occurred in clinical trials to date. Currently, we are continuing to conduct one Phase 3 clinical trial in preventive treatment of migraine, and the long-term safety study as well as one Phase 1 clinical trial, with one more Phase 1 clinical trialexpected to commence in the second quarter of 2019. These Phase 1 trials included evaluation of important drug-drug interactions looking at the effect of administering itraconazole, rifampin or fluconazole on the pharmacokinetics ("PK") of rimegepant. Also included are population studies to evaluate any differences seen in PK in patients with hepatic or renal impairment, cardiac conduction effects, as well as differences in PK that could be seen in the elderly.

As of February 2019, over 3,500 patients have been administered rimegepant across all studies. In completed Phase 2 and Phase 3 rimegepant clinical trials, for which all subjects have completed treatment, SAEs have been reported with none of these SAEs considered to be related to study drug. In total, we believe the current data suggests a favorable benefit-risk profile for rimegepant in the acute treatment of migraine attacks. The clinical experience with rimegepant to date has allowed the characterization of safety and tolerability at substantial multiples of the intended therapeutic dose and intended frequency of use. Rimegepant has been assessed in single doses up to 1500 mg and in multiple doses from 75 mg to 600 mg with 14 days of dosing (including 300 mg twice daily), where the higher doses yielded exposures more than 54 times greater in area under the curve ("AUC"), which is a measure of drug exposure, and 23 times higher in $C_{max}$, which is the peak concentration that a drug achieves after dosing, as compared to the mean therapeutic exposure of a single 75 mg dose. These high exposure multiples were observed to be generally well tolerated.

Since no data are available regarding the effects of rimegepant on human fetuses or newborns, women of childbearing potential must use adequate birth control and have a negative serum or urine pregnancy test to be eligible to receive rimegepant. Female subjects should avoid attempts at pregnancy in the month prior to exposure to rimegepant and eight weeks after exposure to rimegepant. All urine pregnancy testing results must be confirmed by serum pregnancy testing. Drug interaction studies with oral contraceptives demonstrated modest increase in exposure to estrogen and norelgestromin upon multiple doses of rimegepant 75 mg. Co-administration of rimegepant with oral contraceptives was safe and well tolerated. These results enabled enrollment of women of child bearing potential receiving oral contraceptives to be enrolled in the Phase 3 studies.

***Nonclinical Toxicology***

Rimegepant is not genotoxic or phototoxic and has a low potential for off-target receptor interactions or effects on the cardiovascular, respiratory, and central nervous systems ("CNS"). With repeated dosing up to three months, rimegepant was clinically tolerated at up to 150 mg/kg/day in rats and 100 mg/kg/day in monkeys. No histopathologic liver findings were noted in monkeys treated for 3 months at all doses (the highest dose yielded an AUC exposure that was 120× the anticipated human AUC at a therapeutic dose of 75 mg/day). The liver was the primary target organ in mice at levels of 100 mg/kg/day and greater and in rats at levels of 60 mg/kg/day and greater. These dosing levels were not associated with hepatocellular degeneration

/necrosis, inflammation, or fibrosis. In monkeys treated for 3 months, target organ effects were limited to minimal to moderate macrophage accumulation (histiocytosis) in mandibular and mesenteric lymph nodes (considered to be a marginal exacerbation of a common spontaneous change in this species) at 100 mg/kg/day. Hepatic lipidosis identified in mouse and rat studies was determined to be rodent specific as it was not observed at rimegepant exposures in monkeys which overlapped those producing lipid effects in rats in the three-month pivotal studies. At the NOEL (no observable effect level) and NOAEL (no observable adverse effect level) doses in rats (30 mg/kg/day) and monkeys (50 mg/kg/day) in the three-month studies, mean (male and female combined) AUC exposures were at least 23× (for rats) and 56× (for monkeys) the anticipated human AUC at a 75 mg/day clinical dose. Since fetal effects in rats were observed only at doses that produced maternal toxicity (300 mg/kg/day) and there were no fetal findings in rabbits at any dose level, rimegepant is not considered to be a selective developmental toxicant.

In a 6-month rat study, animals were administered rimegepant orally at daily doses of 0, 20, or 45 mg/kg/day. The NOAEL was the high dose, 45 mg/kg/day with no evidence of toxicity at any dose. In a 9-month cynomolgus monkey study, animals were administered rimegepant orally at daily doses of 0, 15 or 50 mg/kg/day. The NOAEL was the high dose, 50 mg/kg/day with no evidence of toxicity at any dose level. Chronic administration to rats (6 months) and monkeys (9 months) demonstrated NOAEL values at doses of 45 and 50 mg/kg/day, respectively. Exposures were at least 29X (rat) and 17X (monkey) the anticipated human AUC at a 75 mg/day clinical dose.

***Our Product Candidate BHV-3500, a CGRP Receptor Antagonist for Acute and Preventive Treatment of Migraine***

BHV-3500 is the second compound from our CGRP receptor antagonist platform and represents a novel chemical structure compared to other small molecule CGRP receptor antagonists in development (including rimegepant). We are developing BHV-3500 for the acute and preventive treatment of migraine, with initial studies being conducted in acute treatment, and we believe it has the potential to improve the existing standard of care based on the following benefits:

- **Multiple Potential Routes of Delivery**—BHV-3500 may be used by nasal, subcutaneous, inhalation or potential oral routes of administration with rapid onset of treatment effect, compared to the anti-CGRP monoclonal antibodies ("mAbs") that are currently available which have a more cumbersome route of administration to patients in the form of intravenous or subcutaneous use. The first formulation of BHV-3500 in clinical trials is for intranasal delivery that will be assessed for rapid onset of action in the acute treatment of migraine.

- **Favorable Safety Profile**—Like rimegepant, we believe BHV-3500 will have a favorable safety and tolerability profile in the clinic, attributable to multiple properties such as its high selectivity for the CGRP receptor, low propensity to aggregate in lipids, and its expected excretion from the body in a largely unchanged state. Unlike other small molecule CGRP receptor antagonists that show potential for liver effects at high exposures, BHV-3500 has not demonstrated any propensity for liver abnormalities in preclinical studies to date, even at very high dose levels. Because preventative treatments involve chronic dosing on a daily basis, any potential target organ effects on the liver could be problematic. Therefore, based on these observations from nonclinical toxicology studies, we believe that BHV-3500 may provide a substantial benefit over other agents with such propensities. In addition, in preclinical studies of BHV-3500, no significant cardiovascular safety or systemic toxicity issues were observed, in contrast to sumatriptan, which displays dose-dependent vasoconstriction.

- **Superior Chemical Attributes**—BHV-3500 is a highly soluble, potent antagonist at the human CGRP receptor. Because BHV-3500 exhibits an *in vitro* and *in vivo* efficacy profile similar to rimegepant, we believe that BHV-3500 will also have a comprehensive (pain, nausea, photophobia and phonophobia) and durable efficacy profile. The chemical attributes of BHV-3500 also allow for a variety of formulations that may provide a more rapid onset of efficacy. Unlike mAbs, which are large biologic molecules, BHV-3500 is a small molecule that directly binds with high potency to the human CGRP receptor.

- **Higher Value to Patients and Payors with Lower Expected Cost Compared to Biologics**—We expect that as a small molecule, BHV-3500 will have a lower cost of goods than mAbs, which are biologics.

- **Potential for Multiple Indications**—Although its nonclinical safety and efficacy profile suggests BHV-3500's potential for daily administration and development for prevention of migraine, we believe this compound also has the potential to be developed in the acute treatment of migraine. BHV-3500 adds flexibility to our CGRP development program as a stand-alone agent for prevention therapy or a complementary intranasal formulation for rapid onset of action in the acute treatment of migraine.

We believe BHV-3500 has the potential to address a significant unmet need in the acute treatment of migraine in patients by delivering a faster onset of action and relief of migraine. This profile will enable it to compete effectively with current and future migraine therapies. BHV-3500 may afford multiple routes of delivery including intranasal delivery and daily oral

administration for acute and preventative treatment of migraine, potential for enhanced safety profile, superior chemical attributes and a higher value to patients and payors with lower expected costs compared to large molecule biologics in current development.

*Clinical Development Plans*

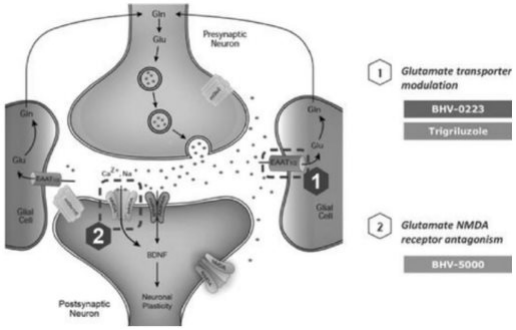
Administration of intranasal BHV-3500 in a Phase 1 clinical trial was initiated in October 2018 and has achieved targeted therapeutic exposures. The compound is expected to advance into a Phase 2/3 trial to evaluate efficacy for the acute treatment of migraine in 2019. We believe that intranasal BHV-3500 may provide a ultra-rapid onset of action that could be used in a complimentary fashion with other migraine treatment when the speed of onset is critical to a patient. We are also planning to initiate a Phase 2 proof of concept trial in the second quarter 2019 to evaluate the safety and efficacy of rimegepant in patients with treatment refractory trigeminal neuralgia at the Johns Hopkins University School of Medicine.

**Our Glutamate Platform**

We are developing three product candidates, troriluzole, BHV-0223 and BHV-5000, that modulate the glutamate system via two distinct mechanisms which form the basis of our glutamate platform—glutamate transporter modulators (troriluzole and BHV-0223) and glutamate *N*-methyl-D-aspartate ("NMDA") receptor antagonists (BHV-5000).

Glutamate is an important neurotransmitter present in over 90% of all brain synapses and is a naturally occurring molecule that nerve cells use to send signals to other cells in the central nervous system. Glutamate plays an essential role in normal brain functioning and its levels must be tightly regulated. Abnormalities in glutamate function can disrupt nerve health and communication, and in extreme cases may lead to nerve cell death. Nerve cell dysfunction and death leads to devastating diseases, including ataxia, ALS and other neurodegenerative disorders. Glutamate clearance is necessary for proper synaptic activation and to prevent neuronal damage from excessive activation of glutamate receptors. Excitatory amino-acid transporters ("EAATs"), help regulate glutamate clearance, and are responsible for most of the glutamate uptake within the brain.

The mechanism of action of our glutamate platform is depicted below. Glutamate must be tightly regulated once released from a pre-synaptic neuron and acts as a signaling neurotransmitter to stimulate the post-synaptic neuron via stimulation of glutamate receptors (e.g., NMDA, AMPA or Kainate receptors). Glial cells surrounding the synaptic junction are predominantly responsible for clearing glutamate through transporters, the EAATs. There are five distinct types of glutamate transporters. (1) As depicted in the glial cell to the right of the figure below, BHV-0223 and troriluzole increase the activity of the EAATs to increase the clearance of glutamate and decrease glutamate release from the pre-synaptic neuron. Troriluzole and BHV-0223 also inhibit presynaptic ion channels that may inhibit the release of glutamate from presynaptic neurons. (2) As depicted in the postsynaptic neuron to the bottom of the figure below, BHV-5000 blocks glutamate signaling that is mediated by post-synaptic NMDA receptors. Modulating glutamate also has the potential to be neuroprotective and increase the release of neurotrophic factors, including brain derived neurotrophic factor ("BDNF") which are endogenous molecules that help to support the survival of existing neurons, and encourage the growth and differentiation of new neurons and synapses.



***Glutamate Transporter Modulation***

Abnormal glutamate release or dysfunction of glutamate clearance can cause overstimulation of glutamate receptors which can lead to a dangerous neural injury called excitotoxicity, which has been associated with a wide range of neurodegenerative diseases. The FDA has approved anti-excitotoxicity drugs that act on the glutamatergic system by blocking NMDA receptors, such as memantine ("Namenda") for Alzheimer's disease, lamotrigine ("Lamictal") for epilepsy and bipolar disorder and riluzole ("Rilutek") for ALS. Although these drugs show the therapeutic potential of glutamate receptor antagonists in the treatment of a range of neurological diseases, many of these approved drugs have serious side effects and other drawbacks that we have attempted to solve with our development of BHV-0223 and troriluzole.

We are currently developing troriluzole as a potential FDA-approved drug treatment option for patients suffering from obsessive compulsive disorder ("OCD"), Alzheimer's disease, ataxia (initially focusing on SCA) and Generalized Anxiety Disorder ("GAD"). We commenced a Phase 2/3 double-blind, randomized controlled trial on the use of troriluzole in OCD in December 2017, which is expected to complete enrollment in 2019. In addition, a Phase 2/3 double-blind, randomized controlled trial of troriluzole in the treatment of mild-to-moderate Alzheimer's disease in collaboration with the Alzheimer's Disease Cooperative Study, a consortium of sites funded by the National Institutes of Health, is currently enrolling study subjects. A futility analysis will be conducted when approximately 100 randomized subjects have reached approximately 24 weeks of dosing, by the end of 2019. The 48-week extension phase of the SCA Phase 2/3 trial is complete and the extension phase has been expanded to 96-weeks. We expect to receive the data from that portion of the trial by the end of 2019. The Phase 2/3 double-blind, randomized controlled trial of troriluzole in GAD has started enrolling subjects and is expected to complete enrollment in 2019.

OCD is a chronic neuropsychiatric disorder characterized by symptoms of obsessions (intrusive thoughts) and compulsions (repetitive behaviors) that can interfere with patients' functional abilities. According to the National Institute of Mental Health, the 12-month prevalence of OCD is 1% of the U.S. adult population, and approximately half of these cases are characterized as severe. First-line treatment for OCD includes cognitive behavior therapy, selective serotonin reuptake inhibitors ("SSRIs") and adjunctive use of atypical antipsychotics. Nonetheless, up to 60% of patients have an inadequate response to conventional intervention strategies. While SSRIs and atypical antipsychotics have been approved for OCD, the majority of patients do not have an adequate response to pharmacologic treatment, and some seek invasive neurosurgical procedures to ameliorate symptoms. Despite the significant public health burden, no novel mechanisms of action have been approved by the FDA for OCD in over two decades. The rationale for use of troriluzole in OCD is supported by clinical data with its active metabolite, riluzole, in populations with OCD in open-label and placebo-controlled clinical trials as well as in preclinical, genetic and neuroimaging studies implicating the glutamatergic hyperactivity in the pathogenesis of OCD.

Alzheimer's disease is the most common form of dementia, characterized by symptoms of progressive memory loss and impairment in other areas of cognition. According to the Alzheimer's Association, approximately 5.5 million people in the United States are affected by the disease and, with the aging population, that number is expected to triple by 2050. We believe the rationale for the study of troriluzole in Alzheimer's disease is supported by preclinical studies on the active metabolite, riluzole, in multiple relevant preclinical models and our own clinical data from the Phase 2/3 clinical trial on the potential of troriluzole to overcome limitations of administering riluzole.

SCA represents an orphan disease. According to a 2016 report by Orphanet cataloging the prevalence and incidence of rare diseases, SCA affects approximately 22,000 individuals in the United States. We have received both orphan drug designation and fast track designation from the FDA for troriluzole for the treatment of SCA. In October 2017, we reported topline data from the 8-week randomization period from the Phase 2/3 clinical trial in SCA. At the eight week time point, troriluzole did not statistically differentiate from placebo. Post-hoc analyses suggested the potential for favorable therapeutic effects of troriluzole, based on numerically superior treatment effects compared to placebo in groups of subjects with less inherent pre-randomization variability on the primary endpoint and also in those, who based on baseline characteristics, would be expected to have greater drug exposures. In the trial, we observed a favorable safety and tolerability profile. For example, no subjects demonstrated an elevation of liver transaminases of 3-fold or greater than the upper limit of normal; whereas, a similar exposure of the active metabolite, riluzole, is associated with about an 8% rate of such elevations, based on the Rilutek Prescribing Information. The 96-week extension phase of the SCA trial is ongoing, and we are continuing to assess the data from the trial. Based on post-hoc analyses we are in active dialogue with the FDA to discuss the potential for further development of troriluzole in ataxias and the FDA has expressed willingness to accept a modification of our trial's primary endpoint, the Scale for Assessment and Rating of Ataxia ("SARA"), as an acceptable registrational endpoint.

GAD represents a disorder of significant unmet need, affecting approximately 4.3% of the population at some point in their life. Approximately one-third of cases are considered severe. GAD is a chronic condition characterized by excessive anxiety and worry that is out of proportion to actual context and causes significant distress or functional impairment. Rates of full remission have been observed to be low, with recovery rates from the index episode of less than 60% after a 12-year follow-up. In clinical studies of approved treatments (selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors) the rates of remission are typically less than 50%. The social impact includes increased risk of not marrying, absenteeism, increased risk of suicide, and high healthcare costs. Minimal research has been conducted on the treatment of

GAD that has not responded to conventional therapy. Frequently treatment-resistant patients are adjunctively administered benzodiazepines despite the potential for abuse and consequently symptom exacerbation. Based on the unmet medical need described above, additional treatments are required for populations with GAD that has not responded adequately to pharmacotherapy.

In addition, preclinical and small-scale pilot studies are underway to explore troriluzole's use in the treatment of a pipeline of other indications such as some cancers whose spread is thought mediated by glutamate transmission, such as melanoma and glioblastoma. We are also developing analogs of troriluzole and other related prodrugs for potential use in these indications.

An NDA for ALS was filed for BHV-0223 with the FDA in September 2018 with the Prescription Drug User Fee Act ("PDUFA") date of July 2019. According to the ALS Association, ALS affects up to 20,000 individuals in the United States and according to industry data, we estimate 15,000 individuals are clinically diagnosed, with 7,500 ALS patients actively treated with generic riluzole or branded Rilutek. As the first of two drugs approved by the FDA for the treatment of ALS and the only drug to extend life and/or time to tracheostomy, riluzole is the established standard of care. However, while the market is highly genericized, there have been limited further clinical improvements or advances in ALS riluzole therapeutics since the FDA's approval in 1995. In addition, the use of riluzole is limited by a number of non-desirable attributes. We have received orphan drug designation from the FDA for BHV-0223 in ALS and we have observed results suggesting bioequivalence to Rilutek in a recently completed Phase 1 clinical trial. We believe that BHV-0223, if approved, could gain meaningful market share based on its favorable formulation attributes.

BHV-5000 is an orally available, first-in-class, low-trapping, NMDA receptor antagonist prodrug that we are developing for the treatment of neuropsychiatric indications. One of these indications may include Rett syndrome. Rett syndrome is a rare and severe genetic neurodevelopmental disorder. After six to 18 months of apparently normal post-natal development, patients with Rett syndrome develop global deceleration of psychomotor function, loss of acquired cognitive skills and brain-mediated episodes of transient respiratory suppression. With intensive care, patients may survive into adulthood, yet they are severely physically and cognitively impaired. Rett syndrome affects approximately 15,000 individuals in the United States. No approved drug therapies for Rett syndrome are currently available and care is supportive. The rationale for the study of BHV-5000 in Rett syndrome is based on results of studies with BHV-5000, its active metabolite and ketamine in preclinical mouse models, in which improvement in key clinical features of the disease have been observed, including a reduction in the frequency of episodes of respiratory suppression. These preclinical findings are supported by anecdotal clinical reports regarding the use of ketamine, another NMDA receptor antagonist, in patients with Rett syndrome that have been reported to also show clinical improvements. Other potential indications include neuropathic pain and major depression.

***Our Product Candidate Troriluzole for Ataxias, OCD, Alzheimer's Disease and Generalized Anxiety Disorder***

Troriluzole is a new chemical entity ("NCE") and tripeptide prodrug of the active metabolite, riluzole. Based on its mechanism of action, preclinical data and clinical studies, troriluzole has potential for therapeutic benefit in a range of neurological and neuropsychiatric illnesses. Initial development has focused on its use in treating SCA, an orphan neurological indication that currently has no approved drug therapies and for which the active metabolite, riluzole, has demonstrated preliminary efficacy in two prior randomized controlled trials conducted by third parties. We acquired troriluzole from ALS Biopharma, LLC ("ALS Biopharma"), and Fox Chase Chemical Diversity Center, Inc. ("FCCDC"), along with an estate of over 300 prodrugs. A prodrug is a compound that, after administration, is metabolized in the body into an active drug. Troriluzole is actively transported by virtue of recognition of its tripeptide moiety by the PepT1 transporter in the gut, and is responsible for the increased bioavailability of the drug. Once inside the body, the prodrug, troriluzole is cleaved by enzymes in the blood to the active metabolite riluzole. To mitigate the limitations of riluzole, several classes of prodrugs were designed, synthesized, and evaluated in multiple *in vitro* stability assays that predict *in vivo* drug levels. Troriluzole is a third generation of prodrug development and the product of six years of intensive chemistry efforts.

Riluzole is currently only indicated for ALS and has a number of non-desirable attributes that have limited its clinical use. Key limitations of riluzole include:

- **Poor oral bioavailability**—When riluzole is administered in a tablet form, approximately 40% is either not absorbed or is metabolized in the liver before reaching systemic circulation. The fraction that does not reach systemic circulation and does not contribute to efficacy only increases the drug burden to the liver. This is thought to contribute to its negative safety effects, such as the liver effects described below.

- **Only tablet formulation currently available in United States**—It is difficult for many patients with ALS to swallow, as oral and laryngeal dysfunction can be an early symptom of ALS. Such patients may choose to crush the tablets and mix it with food to make them easier to swallow; however, this is thought to decrease bioavailability.

- **Negative food effect**—Riluzole must be taken on an empty stomach, at least one hour before or two hours after a meal, and failure to adhere to these guidelines results in lower drug levels and potentially decreased therapeutic effects. This can be particularly challenging for late-stage ALS patients who require a feeding tube for nutrition.

- **Negative effect on liver**—Riluzole has been shown to have dose-dependent liver effects that include elevations on liver function tests. Taking riluzole necessitates regular laboratory monitoring of liver function. In addition, according to the FDA's warnings and precautions for Rilutek in its U.S. prescribing information, cases of clinical hepatitis, one of which has been fatal, have been reported in patients taking riluzole.

- **Pharmacokinetic variability**—Due to extensive first-pass metabolism and CYP1A2 metabolism, which is heterogeneously expressed and thought to be responsible for the marked pharmacokinetic variability between individuals, riluzole has been observed to have marked pharmacokinetic variability, an attribute that manifests as a wide range of systemic drug exposure in populations administered the same dose.

- **Oral numbness—**Patients have reported oral numbness associated with the active pharmaceutical ingredient riluzole, which makes development of alternate formulations challenging.

The prodrug design and selected administration pathway that was pursued with troriluzole is intended to address all of these limitations of riluzole. In addition, a prodrug can be engineered to enhance absorption and protect from diminished absorption when taken with meals. The troriluzole preclinical development strategy was based on optimizing *in vivo* and *in vitro* features, such as stability in gastrointestinal and stomach fluids; stability in liver microsomes; favorable safety pharmacology with respect to off-target effects (particularly liver effects); metabolic cleavage in the plasma to release the active moiety; and enhanced gastrointestinal absorption properties. In *in vivo* studies in rodents, the intended benefits of this optimization program were observed, including delayed peak concentrations and greater exposure.

After six years of chemistry development and preclinical testing, the resulting lead prodrug from the chemistry program was troriluzole. Troriluzole is chemically comprised of riluzole linked via an amide bond to a tripeptide that is a substrate for gut transporters (PepT1) and which contributes to its improved bioavailability. The tripeptide moiety is cleaved by plasma aminopeptidases, releasing riluzole and naturally occurring amino acids, which we believe are readily managed by endogenous metabolic routes. We believe that the estate of compounds we acquired, combined with our internally developed intellectual property, will provide a significant protection for our innovations. Troriluzole is stable in fluids from the gastrointestinal tract and expected to have a differentiated profile with regard to any liability for hepatic effects.

SCA was chosen as the lead indication based on a strong preclinical rationale as well as demonstration of preliminary efficacy of troriluzole's active metabolite, riluzole, in two randomized controlled trials in patients with SCA and other ataxias conducted by third parties (Ristori 2010; Romano 2015). We continue to develop troriluzole for the treatment of ataxias, with an initial focus on SCA.

*The Potential Benefits of Troriluzole Compared to Riluzole*

We believe troriluzole offers the following potential advantages, compared to orally dosed riluzole:

- **Improved Bioavailability**—Troriluzole is a substrate for the gut transporters (PepT1). This is thought to increase the bioavailability of the drug as compared to orally dosed riluzole, meaning that more of the compound is absorbed by the body into the blood stream and can have an active effect. Studies have shown that administration of agents through peptide transporters significantly increases the absorption of drugs with otherwise poor oral bioavailability.

- **No Negative Food Effect**—Troriluzole shows no food effect in human studies, meaning that the drug will not be associated with special meal restrictions, a phenomenon potentially attributable to enhanced uptake by intestinal transporters specific to the peptide-containing moiety of troriluzole. This is in contrast to oral riluzole tablets, which require a period of fasting around dosing in order to reach therapeutic levels, currently a dose-limiting factor of riluzole.

- **Lower Overall Drug Burden to the Liver**—As a prodrug that mitigates first-pass liver metabolism and enhances bioavailability, therapeutic concentrations of the active metabolite riluzole can be achieved with a lower drug dose as compared to riluzole tablets. In addition, release of the active metabolite over time will result in a reduced bolus hepatic concentration as compared to that associated with riluzole tablets. Taken together, we believe these attributes of troriluzole will reduce the potential for adverse liver effects.

- **Optimized Dosing Regimen and Compliance**—Troriluzole has been developed as a convenient once-daily dose, which could improve regimen compliance for patients. We believe these are important features to optimize long-term health outcomes in the treatment of patients with chronic diseases.

- **Potential for Developing Multiple Formulations**—Troriluzole is highly soluble and does not exhibit the profound oral numbness associated with riluzole tablets. As such, we believe troriluzole has the potential to be developed in multiple formulations including intranasal, subcutaneous, intravenous, sublingual and other forms.

*Overview of Ataxias and Limitations of Current Treatment*

Ataxias are a group of degenerative diseases of the nervous system, including hereditary ataxias and sporadic ataxias. According to the National Ataxia Foundation, the word "ataxia" originates from a Greek word meaning "without order" or "incoordination" and aptly describes many of the symptoms that are experienced by people who suffer from the many forms of ataxia, including problems with coordination, balance and movement which can affect a person's fingers, hands, arms, legs, body, speech and eye movements. Ataxias are generally classified as being either hereditary or sporadic. Hereditary ataxias are degenerative disorders that progress over a number of years. The hereditary ataxias include autosomal dominant forms, such as SCA, episodic ataxias and dentratorubral-pallidoluysian atrophy, and autosomal recessive forms, such as Friedreich's ataxia, fragile X-associated tremor/ataxia syndrome and ataxia-telangiectasia. Sporadic ataxias are generally idiopathic, do not run in families and have an onset later in life. Sporadic ataxias share many clinical features of the hereditary forms, which is thought to be attributable to similar underlying cerebellar dysfunction.

Although symptoms may vary, the typical clinical course of SCA might be described as follows. Balance and coordination are affected first. Incoordination of hands, arms, and legs, and slurring of speech are other common, early symptoms. Over time, individuals with SCA may develop numbness, tingling, or pain in the arms and legs (sensory neuropathy), uncontrolled muscle tensing (dystonia), muscle wasting (atrophy), and muscle twitches (fasciculations). Walking becomes difficult and is characterized by walking with feet placed further apart to compensate for poor balance. Impaired coordination of the arms and hands affects the ability to perform tasks requiring fine motor control such as writing and eating. Rarely, rigidity, tremors, and involuntary jerking movements (chorea) have been reported in people who have been affected for many years. As time goes on, ataxia can affect speech and swallowing. Finally, individuals with SCA may also have difficulty processing, learning, and remembering information (cognitive impairment). Notably, there can also be significant clinical variation in the order and extent of symptom expression between mutations, within a common mutation, and even within a kindred that shares the same genotype. Non-cerebellar involvement may also occur in many SCA subtypes (such as cognition, pyramidal, extrapyramidal, motor neuron, peripheral nerve or macular involvement). Signs and symptoms of SCA typically begin in early adulthood, but can appear anytime from childhood to late adulthood; SCA is degenerative and progresses over a number of years. The neurodegeneration is attributed to the production of abnormal proteins that cause the affected nerve cells, predominantly cerebellar purkinje fibers, to eventually function poorly and ultimately degenerate. As SCA progresses, coordination problems become more pronounced. Atrophy of the cerebellum and sometimes brainstem may be apparent on brain imaging. The diagnosis of SCA requires the exclusion of acquired, non-genetic causes of ataxia, such as alcoholism, vitamin deficiencies, multiple sclerosis, vascular disease, tumors, and paraneoplastic disease. A definitive diagnosis requires genetic testing or occurrence within a kindred that has an identified mutation. Lifespan is significantly shortened due to complications related to neurological deficits.

There are currently no FDA-approved medications for the treatment of SCA or any other cerebellar ataxia, and treatment is supportive. In general, multidisciplinary care provides supportive measures and the goal of this treatment is to improve quality of life and survival.

*Our Clinical Program for Troriluzole in Spinocerebellar Ataxia*

*Phase 1 Trials with Troriluzole*

In July 2016, we began a Phase 1 randomized, double-blind, placebo-controlled study to evaluate the safety, tolerability and PK of single and multiple ascending doses of troriluzole in normal healthy volunteers. In this study, the initial safety and tolerability of troriluzole at single doses ranging from 9.5 mg to 200 mg and multiple doses ranging from 35 mg to 200 mg daily were assessed. Fifty-eight healthy volunteers have been dosed with troriluzole and 20 have been dosed with placebo. Based on preliminary data, both single and multiple doses up to 200 mg have been well tolerated without evidence of novel, clinically significant safety signals or lab abnormalities. There is no apparent dose response regarding the frequency or severity of AEs. In the blinded group, including subjects treated with both placebo and troriluzole, the most common AEs were headache (five subjects, two with moderate severity and three with mild severity) and constipation (two subjects). No pattern of AEs or lab abnormalities has become apparent to provide specific cautions or to suggest cautions beyond what is appropriate for the active metabolite, riluzole. Preliminary results suggest approximately 25% to 30% greater systemic exposure of the active metabolite via oral administration of troriluzole as compared to riluzole tablets. In addition, the time to peak

concentration of the active metabolite via oral administration of troriluzole was extended relative to that achieved with oral riluzole tablets, thus suggesting the mitigation of first-pass metabolism. A cross-over arm of the trial assessing fed and fasted conditions suggested no food effect. These pharmacokinetic properties differentiate from direct oral administration of the active metabolite. These preliminary safety, tolerability and pharmacokinetic data support advancement of troriluzole. Commencing in December 2017, an additional single and multiple dose study was conducted to assess the safety, tolerability and PK of a 280 mg dose in 10 healthy young and elderly volunteers (8 active; 2 placebo). Results support adequate safety and tolerability and yielded mean exposures comparable to what would be expected from a 200 to 250 mg dose of Rilutek (based on extrapolation from Chandu 2010), a dose range that has been safely used in clinic populations and associated with efficacy in a range of disorders in randomized controlled trials (Huntington Study Group Neurology 2003; Lacomblez Neurology 1996). In addition, a bioequivalence study was conducted to bridge a commercial formulation with a Phase 2/3 formulation in 32 healthy volunteers. The commercial formulation was well-tolerated and provided bioequivalent exposure with the Phase 2/3 formulation. Exposures from these recent Phase 1 studies are consistent with an absolute bioavailability of approximately 85% or greater, based on known absolute bioavailabilty of Rilutek of 60%.

Based on the results of our Phase 1 trial with troriluzole and two third-party academic trials that have shown preliminary efficacy of riluzole in cerebellar ataxias, we advanced troriluzole into a Phase 2/3 clinical trial for SCA.

The Phase 2/3 trial has two periods: an 8-week randomized, double-blind, placebo-controlled phase followed by a 96-week open-label treatment. The study is being conducted at approximately 15 sites in the United States. The design of the trial was informed predominantly by an advisory panel of the leading ataxia experts that we hosted in February 2016 as well as the observations from peer-reviewed publications in the scientific literature. 141 subjects were randomized to receive a once-daily dose of either placebo or 140 mg troriluzole. Patients were stratified by diagnosis (genotype) and baseline severity (as measured by the patient's gait SARA score). The primary outcome measure of the trial is the change from baseline in patient SARA score after eight weeks of treatment. The choice of the SARA, a validated scale, as the primary outcome measure was based on the consensus of a panel of national experts, based largely on the validation of the instrument in multiple populations, its effective use in demonstrating efficacy in a trial with riluzole (as shown in the Romano study discussed above), favorable psychometric properties, and its ability to assess a broad spectrum of ataxia-related symptoms. A secondary outcome measure is the patient time to perform an eight-meter walk test. Exploratory outcome measures include improvement as measured using the Unified Huntington's Disease Rating Scale Part IV on functional assessment, Clinical Global Impression of Improvement and the Patient Global Impression of Change. Qualifying subjects have genotypically confirmed diagnosis of the most common SCA subtypes. They must have moderate symptom severity (i.e., SARA scores of 8 to 30 inclusive and be able to walk eight meters without assistance). Almost all subjects who completed the eight-week treatment phase elected to participate in the 96-week open-label extension phase.

We reported topline data from the 8-week randomization period from the Phase 2/3 clinical trial in SCA. At the eight week time point, troriluzole did not statistically differentiate from placebo. After eight weeks of treatment, troriluzole treated subjects demonstrated an improvement of –0.81 points [95% CI: –1.4 to –0.2] on the SARA versus –1.05 points [95% CI: –1.6 to –0.4] improvement in placebo, p-value = 0.52. Placebo response in this genetically defined disorder was higher than expected based upon prior European randomized controlled trials in SCA (Romano et al 2015; Ristori et al 2010). Post-hoc analyses suggested the potential for favorable therapeutic effects of troriluzole, based on numerically superior treatment effects compared to placebo in groups of subjects with less inherent pre-randomization variability on the primary endpoint and also in those, who based on baseline characteristics, would be expected to have greater drug exposures.

In this trial, we observed a favorable safety and tolerability profile of troriluzole, with no drug-related SAEs and low discontinuation rates due to AEs. No randomized subjects demonstrated an elevation of liver transaminases of three-fold or greater than the upper limit of normal; whereas, a similar exposure of the active metabolite, riluzole, is associated with about an 8% rate of such elevations. We believe that the reduced effects on the liver may be attributable to a higher bioavailability that in part reflects mitigated first-pass liver metabolism and enhanced PepT1-mediated absorption. Troriluzole has shown absence of a negative food effect, optimized oral bioavailability and no pattern of clinically significant effects on liver function, presenting a profile that appears distinct from what is described for riluzole in its U.S. prescribing information. This profile, in context of recent Phase 1 data assessing higher doses, will allow for exploration of higher exposures of the active metabolite than allowed by the current Rilutek label.

Post-hoc analyses of the data have led to our continued interest in developing troriluzole in SCA and is also founded on two academic randomized controlled trials studying the active metabolite or troriluzole in diverse populations with cerebellar ataxia. In these two publications, the authors conducted studies of riluzole compared to placebo to assess improvement in patients with ataxias using two different ataxia rating scales. In each study, the authors observed statistically significant improvements in the riluzole treatment groups compared to the placebo groups.

- Ristori et al 2010 demonstrated statistically significant improvement in patients with a variety of cerebellar ataxias: In a paper published in *Neurology* in 2010, Ristori and colleagues reported results from a randomized, double-blind, placebo-controlled trial of patients presenting with cerebellar ataxias of diverse etiologies. Forty subjects were randomized to receive eight weeks of treatment with either placebo or 100 mg riluzole (50 mg riluzole tablets, dosed twice daily). The primary endpoint of the trial was the proportion of patients with a decrease of at least 5 points in the International Cooperative Ataxia Rating Scale (ICARS) after four and eight weeks of treatment, compared with the baseline score. The ICARS quantifies severity of ataxia-related symptoms on a scale of zero to 100, with a higher score indicating greater impairment. The total score is the sum of four subscores which measure a patient's posture and gait (static subscore), limb coordination (kinetic subscore), speech (dysarthria subscore) and oculomotor function (ocular movement subscore). The number of patients with a five-point ICARS drop (the primary outcome measure) was significantly higher in the riluzole treatment group than in the placebo group after four weeks (9 out of 19 versus 1 out of 19; p-value = 0.003) and at eight weeks (13 out of 19 versus 1 out of 19; p-value = 0.001). The patient group treated with riluzole demonstrated superior mean changes on the ICARS scores over eight weeks of treatment as compared to the placebo group (–7.05 versus 0.16; p-value < 0.001). The table below shows the changes in ICARS from baseline in each treatment group after eight weeks of treatment, as well as the change in each subscore category. Only sporadic, mild AEs were reported in the trial. Results from this study suggest that riluzole, which is the active metabolite of troriluzole, may confer acute therapeutic effects after eight weeks of dosing in diverse forms of cerebellar ataxia.

| | **Riluzole Group** | **Placebo Group** | |
|---|---|---|---|
| ***Patients, n (%)*** | **n = 19** | **n = 19** | **P-value** |
| Total ICARS scores | -7.05(4.96%) | 0.16 (2.65%) | **<0.001** |
| Static subscores | -2.11 (2.75%) | 0.68 (1.94%) | **<0.001** |
| Kinetic subscores | -4.11 (2.96%) | 0.37 (2.0%) | **<0.001** |
| Dysarthria subscores | -0.74 (0.81%) | 0.05 (0.4%) | **<0.001** |
| Ocular movement subscores | -0.16 (0.9%) | 0.11 (0.66%) | 0.838 |

**Bold**: Statistical significant over placebo treatment

- Romano et al 2015 demonstrated statistically significant improvement in patients with hereditary cerebellar ataxia (both SCA and Friedreich's ataxia): In an article published in *The Lancet* in 2015, Romano and colleagues described results of a study on the use of riluzole in patients with hereditary cerebellar ataxias over a 12-month period. In this multi-center, double-blind, placebo-controlled trial, sixty subjects diagnosed with either SCA or Friedreich's ataxia (enrolled in a 2:1 ratio) were randomized to receive 12 months of treatment with either placebo or 100 mg riluzole (50 mg tablets of riluzole, twice daily). The primary endpoint was the proportion of patients with a minimum one-point improvement on the Scale for the Assessment and Rating of Ataxia (SARA) after 12 months. The SARA is a validated scale consisting of an eight-item, semi-quantitative performance-based assessment of cerebellar ataxia symptoms that measures impairment on a scale of zero to 40, with a higher score indicating more severe ataxia. This scale was developed to address limitations of the ICARS and has been broadly adopted over the ICARS based on superior practicability, reliability and psychometric properties. Twenty-eight patients were treated with riluzole (19 with SA and 9 with Friedreich's ataxia) and 27 patients were in the placebo group (19 with SA and 8 with Friedreich's ataxia). The proportion of patients in the riluzole treatment group with a decreased SARA score was 14 (50%) versus three (11%) in the placebo group (p-value = 0.002). No severe AEs were reported. Primary and secondary outcome measures are shown in the table below. Mean changes in the SARA scores were reported at three and 12 months of treatment, with riluzole associated with reductions in SARA ratings (1.00 and 1.02 points improvement, respectively) and placebo associated with increases (0.50 and 1.67 points, respectively) and resulting in differences between treatment groups that were statistically significant (p-values of 0.008 and 0.001, respectively). Results from this study suggest the potential efficacy of riluzole, which is the active metabolite of troriluzole, in the treatment of cerebellar ataxia.

| | | **Riluzole Group** | **Placebo Group** | **OR 95% or Mean** | |
|---|---|---|---|---|---|
| ***Patients, n (%)*** | | **n = 28** | **n = 19** | **Difference (95% CI)** | **P-value** |
| **Primary Endpoint**: Proportion of patients with improved SARA score at month 12 | **Yes** | 14 (50%) | 3 (11%) | 8.00 (1.95 to 32.83) | **0.002** |
| | **No** | 14 (50%) | 24 (50%) | | |
| Proportion of patients with improved SARA score at month 3 | **Yes** | 14 (50%) | 7 (26%) | 2.86 (0.92 to 8.89) | 0.066 |
| | **No** | 14 (50%) | 20 (74%) | | |
| Changes in SARA score from baseline | **Month 3** | -1.00 (1.75) | 0.50 (2.28) | -1.50 (-2.59 to 0.40) | **0.008** |
| | **Month 12** | -1.02 (2.15) | 1.67 (2.63) | -2.68 (-3.98 to 1.39) | **0.001** |

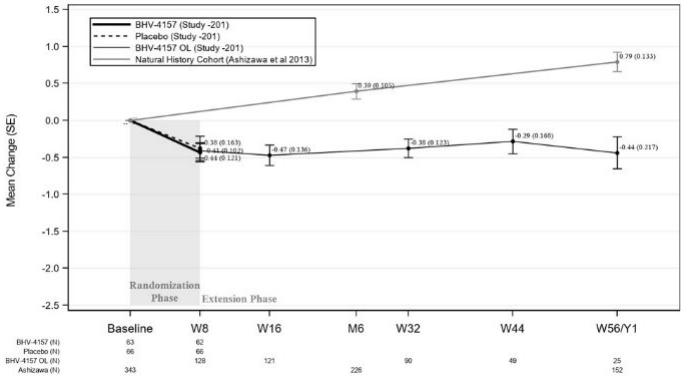
**Bold**: Statistical significant over placebo treatment

Subsequent to our announcement of the topline results from this trial, we engaged in discussions with the FDA regarding the potential for further development of troriluzole in ataxias, and the FDA expressed willingness to consider a modification of our trial's primary endpoint, the SARA, as an acceptable registrational endpoint. The SARA is a scale consisting of an eight-item, semi-quantitative performance-based assessment of cerebellar ataxia symptoms that measures impairment on a scale of zero to 40, with a higher score indicating more severe ataxia. Subsequent post-hoc analyses of the data from the Phase 2/3 trial has shown trends for therapeutic benefit in certain patient subgroups (for example, those who are projected to have higher drug exposures, those with certain genotypes, and those with SARA assessments with more consistent scores prior to randomization). Further, item-specific analyses of the SARA scale data suggest that certain of the eight items measured by SARA were strongly susceptible to a placebo effect. Based upon our analysis of this data, we proposed the use of a modified SARA scale in future clinical evaluation of troriluzole to the FDA. In November 2018 and February 2019, the FDA provided feedback on the use of the SARA scale and definitive guidance on the use of a modified version of the SARA scale, including a reduction in the number of domains measured and simplified scoring categories.

The following chart shows preliminary data from the long term, open-label extension phase of the Phase 2/3 trial after applying a modified SARA scale as compared to data from a natural history reference cohort, to which we applied the same modified SARA scale. A natural history study follows a group of people over time who have a specific medical condition. We utilized data from a published natural history study that enrolled 345 patients with SCA in the United States, and observed the progression of the patients' disease using the SARA scale for up to two years.

In the chart below, interim results from the extension phase (labeled as "BHV-4157 OL") showed sustained improvements in modified SARA scores at all four time periods (extension week 8, 16, 24 and 48) in the troriluzole treated participants, meaning that the mean change in the modified SARA scale was negative at each time point, indicating an improvement or stabilization in ataxia symptoms. In contrast, the natural history reference cohort showed an increase in the modified SARA score, indicating a worsening in ataxia symptoms, when measured at six months and one year. At one year, the mean change in the modified SARA score in the natural history reference cohort was an increase of +0.79, compared to a mean change in the troriluzole cohort of a decrease of −0.44. While the modified SARA scale that we utilized for the analysis includes the same domains as those recommended by the FDA for the planned Phase 3 clinical trial, the response categories differ from the modified SARA scale recommended by FDA, and results from the extension analyses may not be indicative of results utilizing the FDA-recommended modified SARA scale. We believe these observed changes with troriluzole treatment suggest a clinically meaningful benefit relative to the natural history reference cohort.

**Longitudinal Change on Total Modified SARA Scale**




Because we believe that troriluzole may offer therapeutic benefit to patients with SCA and since comparisons to historical controls are generally not accepted by the FDA as the basis for approval, we plan to initiate a second randomized, controlled trial in the first half of 2019 to further evaluate the efficacy of troriluzole in SCA. The clinical observations from our Phase 2/3 trial and open-label extension phase in SCA support our decision to advance troriluzole into an additional randomized, controlled trial that could provide the data needed to serve as the basis for an NDA. This second trial will incorporate trial design modifications based upon our post-hoc analyses of the initial Phase 2/3 trial, and will include: (1) utilization of the

modified SARA scale based on the feedback that we have received from the FDA in November 2018 and February 2019; (2) enrichment of the trial population with particular genotypes; (3) enhanced rater training procedures designed to ensure higher levels of scale reliability; (4) modified dosing regimen; and (5) extension of measurement of the primary endpoint, improvement in the patient's modified SARA scale, to one year.

*Development and Regulatory Pathway*

Our clinical program for troriluzole is based on a regulatory pathway under section 505(b)(2) of the U.S. Food Drug and Cosmetic Act that allows reference to data on riluzole for the purpose of safety assessments. In addition, under current FDA interpretations, we believe troriluzole also qualifies as an NCE and thereby is eligible for conventional regulatory data exclusivities.

We are in active dialogue with the FDA to discuss the potential for further development of troriluzole in ataxias and the FDA has expressed willingness to accept a modification of our study's primary endpoint, the SARA, as an acceptable registrational endpoint. Future directions in ataxia will be based on this interaction and results from the extension phase of the ongoing study.

In the fourth quarter 2017, we completed a study demonstrating the bioequivalence of a commercial formulation of 140 mg troriluzole with the Phase 2/3 formulation that is being used in ongoing studies. An additional Phase 1 study has been conducted to assess the safety, tolerability and PK of higher doses of troriluzole (280 mg daily) in healthy young and elderly adults. We believe the preliminary results suggest an acceptable safety and tolerability profile of this dose and support its exploration in clinical populations.

*Overview of Troriluzole in OCD*

OCD is a chronic neuropsychiatric disorder characterized by symptoms of obsessions (intrusive thoughts) and compulsions (repetitive behaviors) that can interfere with patients' functional abilities. According to the National Institute of Mental Health, the 12-month prevalence of OCD is 1% of the U.S. adult population, and approximately half of these cases are characterized as severe. First-line treatment for OCD includes cognitive behavior therapy, SSRIs and adjunctive use of atypical antipsychotics. Nonetheless, up to 60% of patients have an inadequate response to conventional intervention strategies. While SSRIs and atypical antipsychotics have been approved for OCD, the majority of patients do not have an adequate response to pharmacologic treatment, and some seek invasive neurosurgical procedures to ameliorate symptoms. Despite the significant public health burden, no novel mechanisms of action have been approved by the FDA for OCD in over two decades.

In multiple case studies, the use of riluzole in patients with refractory OCD has commonly been associated with meaningful improvement of symptoms. A small-scale randomized controlled trial in adults with OCD conducted by a third party showed favorable trends for the use of riluzole in outpatient settings but not in inpatient settings, a difference possibly attributed to the intensive therapeutic interactions often available in an inpatient setting. Another randomized controlled third-party study in refractory OCD failed to demonstrate the efficacy of the adjunctive use of riluzole in 60 pediatric patients with refractory OCD. A third randomized controlled third party trial demonstrated statistically significant therapeutic effects with the adjunctive use of riluzole as compared to adjunctive placebo in 50 adults with refractory OCD. These clinical effects are consistent with findings such as genetic associations of glutamate transporter genes with OCD and increased glutamate concentrations in brain and cerebrospinal fluid of patients with OCD. Taken together, we believe there is a clear rationale for advancement of troriluzole or another optimized prodrug of riluzole from our pipeline into a Phase 2 proof-of-concept trial in OCD.

A Phase 2/3 double-blind, randomized controlled trial on the use of troriluzole in adults with OCD commenced in late 2017 and, based on learnings from the Phase 2/3 trial in SCA, employs a higher target dose (200 mg daily) than the study in SCA. Enrollment is expected to complete in 2019. If the results are favorable, we anticipate beginning additional studies necessary to support a NDA.

*Overview of Troriluzole in Alzheimer's Disease*

Alzheimer's disease is a progressive, fatal neurodegenerative dementia. It accounts for up to 80% of dementias. According to the Alzheimer's Association, in 2016 there were approximately 5.5 million people in the United States with the disease, and that number is expected to escalate rapidly in the coming years as the population ages. Observations in multiple preclinical models, suggests the active metabolite of troriluzole protects from Alzheimer's-related pathology and cognitive dysfunction. Reduced glutamate uptake transporters have been reported in postmortem brain tissue of individuals with Alzheimer's disease and the level of glutamate transporter reduction correlates with cognitive impairment as well as markers of synaptic density and neurodegeneration. Preclinical studies also suggest that age-related memory impairment in rats correlates with decreased glutamate transporter expression and this impairment has been shown to be restored by three-weeks of daily treatment with troriluzole's active drug metabolite. These findings form our rationale for pursuing a Phase 2, proof-of-concept trial of troriluzole in patients with mild to moderate Alzheimer's disease, which we began in July 2018 in collaboration with the Alzheimer's Disease Cooperative Study ("ADCS").

The ADCS is a leading Alzheimer's disease clinical trials research consortium that receives major support from the U.S. National Institute on Aging, a part of the U.S. National Institutes of Health. The ADCS was developed to promote the discovery, development, and testing of new drugs for the treatment of Alzheimer's disease. The randomized controlled trial of troriluzole began in July 2018 and is expected to complete enrollment in the second half of 2019.

*Overview of Troriluzole in GAD*

GAD represents a disorder of significant unmet need, affecting approximately 4.3% of the population at some point in their life. Approximately one-third of cases are considered severe. GAD is a chronic condition characterized by excessive anxiety and worry that is out of proportion to actual context and causes significant distress or functional impairment. Rates of full remission have been observed to be low, with recovery rates from the index episode of less than 60% after a 12-year follow-up. In clinical studies of approved treatments (selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors) the rates of remission are typically less than 50%. The social impact includes increased risk of not marrying, absenteeism, increased risk of suicide, and high healthcare costs. Minimal research has been conducted on the treatment of GAD that has not responded to conventional therapy. Frequently treatment-resistant patients are adjunctively administered benzodiazepines despite the potential for abuse and consequently symptom exacerbation. Based on the unmet medical need described above, additional treatments are required for populations with GAD that has not responded adequately to pharmacotherapy.

Our rationale for advancing troriluzole into a Phase 2 trial in GAD is based on treatment effect in preclinical models of anxiety as well as favorable open-label case studies of patients treated with riluzole and a recent randomized, double-blind placebo-controlled crossover trial with BHV-0223 in a clinical model of anxiety disorder. In one case study of riluzole in GAD, eight of 15 patients demonstrated a remission with a median response time of 2.5 weeks after starting riluzole 50 mg twice daily.

*Overview of Troriluzole in Other Indications*

Given the novel chemical properties of troriluzole and its unique mechanism of action, we believe troriluzole, or another optimized prodrug of riluzole, has the potential for broad applicability across several neurological indications where modulation of brain glutamate has been implicated in underlying disease states. A brief description of potential indications that we could pursue in the future with troriluzole or other optimized prodrugs from our pipeline is summarized below. We will determine the timing and prioritization of additional indications as warranted by emerging data.

*Other Orphan Indications*

If data from the ongoing extension phase of the SCA trial support the role of troriluzole in the treatment of SCA, then we will explore the role troriluzole in the treatment of other ataxias. Of note, preliminary data is also provided by the Ristori and Romano randomized controlled trials, which showed improvement in some patients with Friedreich's ataxia, multisystem atrophy of the cerebellar type, sporadic ataxia, antibody-associated ataxia and fragile X-associated tremor/ataxia syndrome. We expect that the next wave of ataxia indications we would pursue, if warranted by data from the SCA trial, would include Friedreich's ataxia and sporadic ataxia.

- *Friedreich's Ataxia:* Friedreich's ataxia is an autosomal recessive disorder associated with progressive cerebellar degeneration with worsening ataxia, areflexia, which is the absence of reflexes, sensory loss, weakness, glucose dysregulation, and cardiomyopathy—often with onset in early childhood. According to the Friedreich's Ataxia Research Alliance, an estimated 6,400 individuals in the United States have Friedreich's ataxia. Treatment is supportive and no pharmacotherapies are approved by the FDA for the treatment of Friedreich's ataxia.

- *Sporadic Ataxia:* Sporadic ataxia, also called idiopathic ataxia, shares symptoms of SCA but is associated with an unknown cause, typically presenting after the age of 40 years and commonly associated with cerebellar degeneration. Sporadic ataxia comprises the majority of patients treated in specialty ataxia clinics. These patients typically have progressive balance difficulties with other features of cerebellar disease such as dysarthria (speech problems), dysphagia (swallowing difficulty), as well as visual symptoms such as double vision. According to Orphanet, the prevalence of sporadic ataxia is between 1 and 9 per 100,000 persons, suggesting that there are between 3,200 and 28,000 individuals with sporadic ataxia in the United States.

*Other (Non-Orphan) Cerebellar Disorders*

- *Essential Tremor:* Like SCA, the pathophysiology of essential tremor ("ET") reflects underlying cerebellar dysfunction. ET is the most common type of tremor, characterized by action and postural tremor in the upper extremities and/or head and voice tremor. The prevalence of ET is approximately four times that of the second most common tremor disorder, Parkinson's disease. ET can be highly disabling, as many ET patients cannot write, type, drink, or feed themselves due to tremor. ET is a progressive disease and with time, the tremor becomes more severe and disabling. Currently, only two medications, primidone and propranolol, are commonly employed as first-line symptomatic treatment of ET, but these are ineffective in 40% of ET patients and none of the available medications are FDA-approved for ET. Therefore, a novel symptomatic therapy for ET could serve an important unmet medical need for a substantial population. Preclinical studies with troriluzole in mouse genetic and toxicity models of ataxia have shown reductions in tremor. Supported by this data, we are developing a Phase 2 study of troriluzole in subjects with ET in collaboration with the Tremor Research Group, a national, independent, non-profit organization of scientific investigators.

*Broader Neuropsychiatric Indications*

Based upon preclinical and preliminary clinical work, we also believe there are several potential expansions for troriluzole, or another optimized prodrug of riluzole from our pipeline, including potential for therapeutic application in a broad range of neuropsychiatric conditions, such as anxiety disorders, mood disorders and neurodegenerative disorders.

Anxiety Disorders

- *Social Anxiety Disorder:* Social anxiety disorder ("SAD"), is a marked and persistent fear of social situations, causing impairment and distress, which can impair school, work and social functioning. SAD affects approximately 12% of Americans. Roughly one-third to one-half of patients with SAD do not experience significant clinical benefit from current treatments, including SSRIs. Several uncontrolled trials have suggested the efficacy of glutamate modulating agents for reducing anxiety symptoms in adults with other anxiety disorders, such as GAD and OCD, as well as major depression. We are collaborating with researchers at Yale University ("Yale") to explore the use of our glutamate modulating agents in the treatment of SAD.

Mood Disorders

- *Bipolar Depression:* Bipolar disorder is a chronic disorder associated with periods of depressive or manic moods that often severely affect overall functioning. The limited available treatment options include conventional antidepressants, but they are associated with increased cycling between manic and depressed phases. Approved agents for bipolar depression (atypical antipsychotics) are associated with weight gain, sedation and safety issues. According to the National Institute of Mental Health, bipolar disorder affects approximately 5.7 million Americans, or about 2.6% of the U.S. population, every year. As many as one in five patients with bipolar disorder commits suicide. The rationale for assessing troriluzole in treating bipolar depression derives from multiple third-party publications on the use of riluzole. In one study of 14 patients with bipolar depression, improvement was observed after treatment with riluzole (and within a subset of four patients that were resistant to lamotrigine, three remitted or partially responded). Another third-party study observed positive effects in 14 largely treatment-resistant patients after six weeks of treatment with 100-200 mg per day of riluzole. In this study, early changes observed on magnetic resonance spectroscopy, which measures patients' brain glutamate levels, correlated with clinical improvement.

*Other Indications Being Pursued by our Collaborators*

Our collaborators are exploring the potential applicability of troriluzole beyond cerebellar and neuropsychiatric indications, including in melanoma (Rutgers University) and glioblastoma (Johns Hopkins University). The oncology collaborations with Rutgers and Johns Hopkins are based upon the mechanistic rationale that some tumors overexpress glutamate receptors, the central role that glutamate may have in cancer metabolism and the effect of glutamate on the tumor microenvironment. Troriluzole is currently being assessed in a Phase 1 study (NCT03229278) to evaluate the safety in combination with nivolumab and pembrolizumab in patients with metastatic or unresectable cancer (including melanoma). The study is being conducted at Rutgers University.

***Our Product Candidate BHV-0223 for ALS***

*Overview of Amyotrophic Lateral Sclerosis and Limitations of Current Treatments*

ALS is a progressive neurodegenerative motor neuron disease that affects nerve cells in the brain and the spinal cord. The disease belongs to a group of disorders known as motor neuron diseases, which are characterized by the gradual degeneration and death of motor neurons. ALS affects up to 20,000 individuals in the United States and typically presents in patients with painless muscle weakness, trouble swallowing and muscle atrophy that ultimately progresses to paralysis, impaired breathing and death.

Since the FDA's approval of riluzole in 1995, only two agents have been approved by the FDA in ALS drug therapeutics and riluzole is the only agent indicated to enhance survival and/or time to tracheostomy. Several therapies are currently in clinical trials. Riluzole itself has pharmacokinetic and pharmaceutic limitations that have restricted its broader clinical application. Riluzole tablets have 60% bioavailability, attributed to high first-pass metabolism in the liver that is thought to be mediated via metabolism by the heterogeneously expressed CYP1A2 enzyme. This metabolic route is also thought to contribute

to the high pharmacokinetic variability associated with riluzole. In addition, riluzole is associated with reduced exposure when taken with meals, or a negative food effect, resulting in the guidance to take riluzole within a period of fasting (one hour before or two hours after a meal) for each of two daily doses. In addition, riluzole has dose-dependent effects on liver function tests that necessitate periodic liver function test monitoring and is associated with transient liver transaminase elevations. At riluzole daily doses of 100 mg, drug discontinuation is required in 2% to 4% of subjects. However, this has not been observed with lower doses, an important observation as the planned commercial dose of BHV-0223 represents a lower drug load than the FDA-approved dose of riluzole while delivering similar exposures. The drug substance of riluzole itself has other intrinsic limitations that complicate the ability to produce non-tablet formulations, including very low solubility in water, poor oral palatability, pH dependent chemical stability and intense oral numbness if administered directly to the oral mucosa.

*Our Clinical Program for BHV-0223 in ALS*

BHV-0223 is a formulation of riluzole designed to advance beyond the limitations of riluzole tablets for application in ALS. BHV-0223 is a sublingual ODT of riluzole, that makes use of proprietary Zydis ODT technology that we have licensed from Catalent for use with riluzole. Catalent's ODT technology allows us to develop a form of riluzole that is fast-dissolving and which we expect will mitigate many of the shortcomings associated with the solid oral dosage form of riluzole. Based on over 20 years of global clinical experience with riluzole, we expect that BHV-0223 is likely to be well tolerated in chronic dosing. To date, we have conducted two Phase 1 trials of BHV-0223 in healthy volunteers.

We believe BHV-0223 offers the following potential advantages, compared to the solid oral dosage form of riluzole, in the treatment of ALS:

- **Ease of Administration**—An early symptom in many patients with ALS is difficulty swallowing, which makes it especially challenging for ALS patients to swallow traditional riluzole tablets. In contrast, using our licensed ODT technology, ALS patients will benefit from a fast-dissolving tablet that does not require swallowing or administration of liquids.

- **More Predictable Pharmacokinetic Performance**—Because some ALS patients experience difficulty swallowing, they often crush their solid riluzole tablets and take with food in order to ease administration, which, in addition to resulting in mucosal numbness, leads to uncertain pharmacokinetic performance as riluzole is supposed to be administered on an empty stomach. With BHV-0223, ALS patients will not have to crush or alter the form of administration, leading to more predictable pharmacokinetic performance. In our Phase 1 trials, we have observed that BHV-0223 is associated with less pharmacokinetic variability than 50 mg riluzole.

- **Lack of Food Effect on Overall Exposure (as assessed by AUC)**—Prescribing instructions for riluzole tablets state that it should be taken at least an hour before, or two hours after, a meal to avoid food-related decreases in bioavailability. Patients who do not strictly adhere to these fasting requirements or administer crushed riluzole in food may not be obtaining desired therapeutic levels of riluzole. BHV-0223 was designed to readily be absorbed sublingually and directly enter the blood stream without passing through the intestines. Since absorption of BHV-0223 occurs through the vasculature under the tongue, we do not anticipate fasting requirements. We believe this attribute will be particularly beneficial for late-stage ALS patients who require a continuous feeding tube for nutrition. Topline results from a food effect assessment with a Phase 1 study, demonstrated bioequivalent exposure (i.e., overall exposures as measured by AUC) for BHV-0223 40 mg when administered under fed or fasted states. $C_{max}$ concentrations under fed and fasted conditions differed, as is commonly observed with sublingual formulations; however, it is generally thought that efficacy of riluzole is driven by overall extent of exposure (AUC).

- **Reduced Drug Load and Liver Exposure**—Riluzole is associated with dose-dependent liver function increases attributable to high dose loads and extensive liver metabolism. Since BHV-0223 is sublingually absorbed, first-pass liver metabolism is mitigated and lower doses of riluzole are needed to be administered, thereby reducing potential risk for hepatic enzyme elevations.

BHV-0223 has been dosed in approximately 150 healthy subjects in Phase 1 studies and in patients with ALS for the assessment of pharmacokinetics, safety and tolerability. AEs have generally been mild and transient; no treatment-related SAEs have been observed. In January 2018, we announced topline results of a bioequivalence study. Topline results confirmed that sublingual BHV-0223 (40 mg) achieves bioequivalent exposures relative to Rilutek (50 mg). In the study, 138 healthy volunteers were administered BHV-0223 and Rilutek under fasted conditions. In the pre-specified primary analysis, BHV-0223 achieved area-under-the-curve and peak exposures of approximately 90% and 113%, respectively, compared to those generated by generic riluzole. The 90% confidence intervals were within the 80% to 125% range that is used to define bioequivalence. In this study, 67 of these 138 subjects were also assessed after being administered BHV-0223 (40mg) under fed conditions. Topline results from a food effect assessment with a Phase 1 study, demonstrated bioequivalent AUC exposures for BHV-0223

40 mg when administered under fed or fasted states. Cmax concentrations under fed and fasted conditions differed, as is commonly observed with sublingual formulations; however, it is generally thought that efficacy of riluzole is driven by overall extent of exposure (AUC). In addition, we completed dosing in three other studies: assessing tolerability of a single dose in dysphagic patients with ALS; assessing the tolerability of BHV-0223 with two-month dosing in ALS patients; and, assessing swallowing mechanics via videofluorscopic imaging in healthy volunteers after a single dose of BHV-0223. Results from these studies show that BHV-0223 is generally well tolerated and can be safely administered to patients with ALS and healthy volunteers, without evidence for novel adverse events that have not already been associated with Rilutek tablets. BHV-0223 is associated with higher rates of oral numbness (transient and generally mild) than Rilutek tablets, as expected due to the route of administration.

*Development and Regulatory Pathway*

In December 2016, the FDA granted orphan drug designation of BHV-0223 for the treatment of ALS, with eligibility for orphan exclusivity contingent on a showing that BHV-0223 is clinically superior to Rilutek, a previously approved form of riluzole, as well as any other versions of riluzole that may be approved for the same indication before BHV-0223 is approved. Clinical superiority may be demonstrated by showing that a drug has greater effectiveness than the approved drug, greater safety in a substantial portion of the target population, or otherwise makes a major contribution to patient care.

After a pre-NDA meeting with the FDA in the first quarter of 2018, we submitted a NDA to the FDA to pursue the regulatory approval of BHV-0223 for ALS under Section 505(b)(2) of the U.S. Federal Food, Drug, and Cosmetic Act in September 2018. The PDUFA date is in July 2019.

**Glutamate NMDA Receptor Antagonism**

An NMDA receptor antagonist is a type of glutamate antagonist that works to inhibit the action of NMDA receptors which may play a role in degenerative diseases that affect the brain. BHV-5000 is an oral prodrug of the intravenous drug lanicemine, also referred to as BHV-5500, both of which we in-licensed from AstraZeneca AB ("AstraZeneca"). In addition to being orally available, BHV-5000 is a first-in-class, low-trapping, NMDA receptor antagonist with differentiating pharmacologic properties from other agents in development targeting this receptor. The unique property of low-trapping antagonists is their ability to uncouple from the NMDA receptor more freely than other agents, a property that is thought to contribute to their mitigated risk of dissociative effects as has been observed in the clinic. Lanicemine, the active metabolite of BHV-5000, binds within the NMDA channel pore and functionally blocks the flow of charged ions through the NMDA receptor complex. Lanicemine was initially advanced by AstraZeneca into clinical trials for the potential treatment of stroke, but this development was discontinued as initial results did not warrant continued development for this indication. We are developing BHV-5000 as a potential best-in-class NMDA receptor antagonist for treatment of neuropsychiatric indications.

***Our Product Candidate BHV-5000 for Neuropsychiatric indications, such as Rett Syndrome***

*Overview of Rett Syndrome and Limitations of Current Treatments*

Rett syndrome is a severe neurodevelopmental disorder resulting from an X-linked dominant gene mutation (MECP2). As a result, it occurs almost exclusively in females. After six to 18 months of apparently normal development, patients with Rett syndrome show global deceleration of psychomotor development and subsequent loss of acquired cognitive and motor skills, such as the loss of speech. Patients may also develop pathognomonic stereotyped hand movement or display autonomic dysfunction such as breathing irregularities, including brain-mediated episodes of transient respiratory suppression, or apneic periods. With intensive care, patients may survive into adulthood, yet they are severely physically and cognitively impaired. Rett syndrome occurs in all racial and ethnic groups and occurs worldwide in approximately 1 in every 10,000 live female births. There are approximately 15,000 females with Rett syndrome in the United States. No approved treatments for Rett syndrome are currently available and care is supportive.

*Our Clinical Program for BHV-5000 in Rett Syndrome*

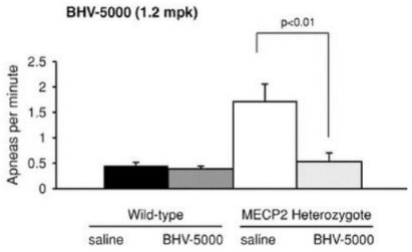
BHV-5000 and lanicemine have been observed to ameliorate the phenotype in transgenic mouse models of Rett syndrome, models which recapitulate key clinical features, such as irregular breathing, apneic periods, abnormal EEG with altered seizure threshold. Based on the preclinical experience, we have chosen to advance BHV-5000 into clinical trials for the treatment of breathing irregularities associated with Rett syndrome. The orally bioavailable prodrug BHV-5000, which was developed as an advancement on the intravenously administered lanicemine, offers an improved route of administration over lanicemine, and has thus been positioned as the lead candidate in this series. After ingestion, BHV-5000 is rapidly cleaved by the enzyme dipeptidyl peptidase-4 (DPP-4), yielding the active metabolite lanicemine. AstraZeneca studied BHV-5000 in a Phase 1 single and multiple ascending dose trial. Doses up to 95 mg of BHV-5000 were studied and were observed to be well tolerated without any clinically relevant safety issues. Among the AEs reported were three cases of euphoria, three cases of hallucination, or visual distortion, and eight cases of nystagmus, a visual condition. These AEs are consistent with NMDA

receptor antagonism. After oral ingestion, systemic concentrations of BHV-5000 were observed to be very low, typically below the limit of quantification.

*Preclinical Studies and Previous Clinical Trials with Lanicemine and BHV-5000*

As noted above, BHV-5000 and lanicemine have been observed to ameliorate the phenotype in transgenic mouse models of Rett syndrome. In particular, BHV-5000 has been observed to reduce the number of apneic episodes that are driven by dysfunctions in the central nervous system. These preclinical findings are consistent with those reported for the NMDA receptor antagonist, ketamine, and have been observed at concentrations that have been well tolerated by healthy volunteers in clinical trials. The potential relevance of the preclinical models with this mechanism of action are supported by anecdotal reports on the incidental use of ketamine in patients with Rett syndrome that have been associated with clinical improvements.

The figure below shows results from a preclinical study with BHV-5000 in a transgenic mouse model. Transgenic (heterozygous for MECP2 mutation) and wild-type mice were administered a single dose of saline or BHV-5000 followed by measurement of apneic episodes. Acute administration of BHV-5000 was associated with a marked reduction in the number of apneic episodes.




Lanicemine has been administered to approximately 770 subjects in single or multiple doses in 18 clinical trials conducted by AstraZeneca and has been observed to be generally well tolerated. In clinical experience with lanicemine, the most common adverse event was dizziness. CNS-type AEs from Phase 1 trials also included headache, somnolence, asthenia, impaired concentration and dysesthesias. In one study, formal assessment of cognitive function in healthy volunteers revealed improvement in some components of memory, decreased vigilance and decreased calmness. Hypotension and hypertension have been reported as AEs, with low mean increases in blood pressure reported in some studies (e.g., 4 - 8 mmHg supine systolic blood pressure; 2 - 4 mmHg supine diastolic blood pressure—which occurred at doses higher than considered necessary for therapeutic effects). AEs related to dissociation were infrequent but more common in the lanicemine group compared to placebo. AEs potentially associated with abuse potential were low but more common in the lanicemine group than the placebo group. No pattern of clinically meaningful differences between lanicemine and placebo were noted on physical exam, clinical laboratory test results or ECG results.

Approximately 40 healthy volunteers have been dosed with single or multiple doses of BHV-5000 in clinical trials conducted by AstraZeneca, and it was observed to be well tolerated without any clinically relevant safety issues. We believe BHV-5000 has no pharmacologic activity of its own and is rapidly metabolized to lanicemine in humans. After oral ingestion, systemic concentrations of BHV-5000 are very low, typically below the limit of quantification.

*Nonclinical Toxicology Experience with Lanicemine and BHV-5000*

In nonclinical studies, the major dose limiting effects in both rats and dogs were central nervous system effects, which appeared rapidly and included ataxia, head weaving, depressed activity, and, at very high doses, convulsions. At pharmacologically effective doses, lanicemine did not elicit adverse effects on learning, memory or attention. Small increases in heart rate and blood pressure at very high doses were observed. In the rat with daily dosing, effects on adrenal gland, heart tissue, thyroid and kidney were apparent at very high doses—more than 10-fold the proposed maximum clinical exposure. These effects were not seen in dogs and intermittent dosing in the rat was not associated with effects on the kidney or heart. At very high doses, evidence of neuron degeneration was apparent in very few neurons, a finding that is associated with glutamate antagonists. Based on these preclinical findings, which were consistent with other NMDA receptor antagonists, such as

ketamine, lanicemine was advanced into clinical trials. Toxicology studies with BHV-5000, up to 2 weeks in rats and dogs, revealed findings consistent with lanicemine, which was expected given the negligible concentrations of BHV-5000 as compared to the active metabolite, lanicemine. A GLP neurotoxicology study is ongoing, as required for this class of agent, in order to confirm maximum acceptable therapeutic exposures in clinic populations.

*Clinical Development of BHV-5000*

In July 2017, we received orphan drug designation from the FDA for BHV-5000 for the treatment of patients with Rett syndrome. Our clinical program for BHV-5000 will build upon AstraZeneca's previous development efforts for lanicemine. In support, BHV-5000 is rapidly metabolized to lanicemine and, in a Phase 1 trial, concentrations of BHV-5000 were detectable in only a few subjects who received the highest dose. As a result, we intend to rely on long-term Good Laboratory Practices ("GLP") toxicology, reproductive toxicology and carcinogenicity studies of lanicemine to potentially expedite the safety package for BHV-5000.

A lead formulation has been selected for advancing into a Phase 1 clinical trial of BHV-5000, to bridge PK with a prior formulation. Enrollment in this study commenced in the fourth quarter of 2017, with the first patient dosed in January 2018. All 10 subjects have been enrolled in a combined single and multiple dose trial (8 active; 2 placebo) and completed study participation. BHV-5000 was observed to be well tolerated with no clinically relevant safety signals. These results are consistent with prior experience. That is, prior formulations of BHV-5000 had been dosed in approximately 40 healthy subjects in a Phase 1 trial conducted by AstraZeneca, and was observed to be well tolerated with no clinically relevant safety signals. Its active metabolite, lanicemine, has been administered intravenously in clinical trials conducted by AstraZeneca to approximately 770 subjects, in single or multiple doses, and has been observed to be generally well tolerated with most AEs being mild and transient in nature.

Currently, we are conducting neurotoxicology studies that are required for NMDA antagonist drugs to define acceptable clinical exposures. Based on these results, an additional Phase 1 study may be required to establish the dose that would subsequently be used in a randomized controlled trial of BHV-5000. One of our planned indications for BHV-5000 is Rett syndrome, based on the ability of BHV-5000 and its active metabolite to favorably impact breathing abnormalities and global brain biochemical abnormalities in transgenic mouse models. The Phase 2/3 trial is being developed in collaboration with experts in the field. Potential other conditions include depression, neuropathic pain and other disorders involving NMDA receptor dysfunction.

*Major Depressive Disorder*

Major depressive disorder ("MDD") is the leading cause of disability worldwide, according to the World Health Organization. In the United States, the prevalence rate is approximately 7%. Despite the approval of over two dozen agents, therapeutic effects are limited. More than one-third of patients who complete an initial course of antidepressant treatment will not achieve a satisfactory response, and as many as 20% of patients have chronic depression despite multiple interventions. The only class of agents approved for this population of inadequate responders (also deemed treatment resistant depression) is atypical antipsychotic medications (e.g., aripiprazole, quetiapine, olanzapine-fluoxetine combination and brexpiprazole), agents associated with significant short-term and long-term side effect burdens (sedation, metabolic syndrome, obesity, extrapyramidal side effects that can include akathisia and elevated risk of tardive dyskinesia). Other agents in clinical stages of development for major depressive disorder include rapastinel (Allergan, in Phase 2 testing), esketamine (Johnson & Johnson, in Phase 3 testing), and ALKS-5461 (a combined formulation of buprenorphine and samidorphin developed by Alkermes, which has reported positive Phase 3 data).

Clinical findings of antidepressant effects of the NMDA receptor antagonist ketamine have provided a link between the NMDA receptor function and depression and a rationale for testing BHV-5000 as an antidepressant. In nonclinical studies, BHV-5000's active metabolite is active in models of depression and anxiety. These data prompted a line of investigation with lanicemine that included four randomized controlled trials conducted by AstraZeneca in patients with treatment resistant depression, overall suggesting an adequate safety and tolerability profile and potential for therapeutic benefit. However, the clinical data to date has not established clear efficacy and additional trials are needed.

*Neuropathic Pain*

Neuropathic pain is a chronic condition caused by dysfunctional or damaged nerves. Neuropathic pain can be a debilitating and common problem affecting approximately 10% of adults in the United States. Despite the availability of multiple approved drugs, including Lyrica, and guidelines for the treatment of neuropathic pain, treatment of this condition remains a major therapeutic challenge. Existing analgesics are often ineffective, can cause serious side effects and have abuse potential that limits widespread use. Increased NMDA receptor activity is known to contribute to central sensitization in neuropathic pain. NMDA receptor antagonists have been shown to reduce hyperalgesia and pain in animal models of neuropathic pain induced by nerve injury and diabetic neuropathy. Clinically used NMDA receptor antagonists, including

ketamine and dextromethorphan, can be effective in patients suffering from neuropathic pain syndromes. The clinical use of robust NMDA antagonists, such as ketamine, is limited due to dissociative, psychotomimetic and abuse potential properties. Novel NMDA receptor antagonists, such as BHV-5000, that are not associated with the psychotomimetic effects and abuse potential could lead to better management of neuropathic pain without causing serious side effects.

**Our Other Platforms**

*Our Product Candidate Verdiperstat for Multiple System Atrophy*

Verdiperstat is a first-in-class, potent, selective, brain-permeable, irreversible myeloperoxidase ("MPO") enzyme inhibitor that we are developing for the treatment of multiple system atrophy ("MSA"). Myeloperoxidase generates an array of cytotoxic oxidants and is a key driver of oxidative and inflammatory processes that underlie a broad range of disorders. MPO is plays a key role in neurodegenerative, inflammatory, and immune-mediated diseases, including MSA, Alzheimer's disease, Parkinson's disease, multiple sclerosis, ischemic and hemorrhagic forms of stroke, epilepsy, depression and other neuropsychiatric disorders. Clinical and experimental studies have revealed the detrimental role of MPO. Hence, suppressing MPO may be a novel treatment approach for these disorders.

Verdiperstat was in-licensed from AstraZeneca (formerly named AZD3241) in September 2018. Seven clinical studies have been completed (all by AstraZeneca), including four Phase 1 studies in healthy subjects, two Phase 2a studies in subjects with Parkinson's disease, and one Phase 2b study in subjects with MSA. In February 2019, we received orphan drug designation from the FDA for the treatment of MSA. Verdiperstat has also received orphan drug designation for the treatment of MSA from the European Commission upon recommendation from the European Medicines Agency's Committee for Orphan Medicinal Products.

*Overview of Multiple System Atrophy and Limitations of Current Treatments*

Multiple System Atrophy

MSA is an orphan disease that is an adult-onset, fatal, neurodegenerative disease characterized by progressive autonomic failure, parkinsonian features, and cerebellar and pyramidal features in various combinations and degrees of severity. It invariably leads to death after an average of 6 to 10 years from symptom onset. No disease-modifying treatment currently exists; only symptomatic and palliative approaches are available.

Multiple system atrophy patients are divided into 2 groups, those with parkinsonian features as the predominant symptoms ("MSA-P") and those for whom cerebellar ataxia is the predominant symptom ("MSA-C"). Approximately 60-80% of MSA patients in Europe and North America have the MSA-P subtype, whereas 65-85% of MSA patients in Japan and Korea have the MSA-C subtype. According to the consensus statement by the American Autonomic Society and American Academy of Neurology in 2007, the diagnosis of MSA includes 3 categories: definite, probable, and possible MSA. Definite MSA requires the neuropathological findings of widespread and abundant CNS α-synuclein-positive glial cytoplasmic inclusions in association with neurodegenerative changes in striatonigral or olivopontocerebellar structures. Probable and possible MSA diagnoses are based on clinical symptoms and neurologic examination findings. The diagnosis of MSA can be aided by laboratory investigations, structural and functional imaging, and a variety of other diagnostic tools. The defining molecular and cellular neuropathology of MSA is the widespread presence of glial cytoplasmic inclusions (GCIs) containing fibrilized α-synuclein protein in oligodendrocytes. Thus, MSA is thus considered an α-synucleinopathy, similar to Parkinson's disease and dementia with Lewy bodies, but with distinct pathological and clinical features. The defining neuropathology of MSA upon postmortem examination includes variable degrees of olivopontocerebellar atrophy and striatonigral degeneration, reflecting the ataxia and parkinsonism, respectively, that are present during life. Neurodegenerative changes affecting the central autonomic nervous system are also evident, and include the hypothalamus, noradrenergic and serotonergic brainstem nuclei, dorsal nucleus of the vagus nerve, nucleus ambiguus, intermediolateral columns of the spinal cord, and Onuf's nucleus. Although the pathophysiological mechanisms underlying MSA remain unclear, evidence from preclinical models and postmortem studies in humans suggest that formation of GCIs is associated with oxidative stress, neuroinflammation, loss of neurotrophic support, and ultimately, neuronal cell death.

Current Treatments

There are currently no approved drugs for the treatment of disease progression in MSA. Existing medical management is focused exclusively on attempting to reduce symptoms by using drugs approved for various other indications along with dietary supplements. Use of these agents in MSA, however, is not supported by high-quality evidence from randomized, double-blind, placebo-controlled trials, and it is widely accepted that none of these drugs is particularly effective in alleviating MSA symptoms.

The dopaminergic agent, levodopa, which is used in Parkinson's disease, is commonly used in MSA at high doses and may reduce motor symptoms, including rigidity and bradykinesia, in a subset of patients. Amantadine is used in MSA and is purported to provide some benefits. Botulinum toxin is used in MSA and may temporarily reduce movement disorder symptoms, such as dystonias. The mitochondrial micronutrient coenzyme Q10 is also used in MSA because of its antioxidant properties. Additional nonspecific measures may be used in MSA to manage autonomic symptoms, sleep disorders, depression, and other clinical manifestations. Non-pharmacological supportive/palliative measures are commonly used in MSA. In terms of motor symptoms, physical and occupational therapy, employment of assistive devices, and speech and language therapy may be used. In terms of autonomic symptoms, intermittent or permanent urethral or suprapubic catheterization may be used for urinary symptoms and elastic stockings and adequate salt and fluid intake may be used for orthostatic hypotension.

The treatment strategies noted above focus on alleviating and managing symptoms rather than modifying the course of MSA. Specifically, there are no medications that can stop, or even slow down, the relentless progression of MSA. In contrast, verdiperstat offers a novel mechanistic approach of reducing MPO activity, which is believed to be involved in the molecular pathogenesis of the disease. This reduction of MPO activity may result in slowing down the progression of MSA.

*Nonclinical Studies and Previous Clinical Trials*

Non-clinical

The nonclinical pharmacodynamics, pharmacokinetics, and toxicology of verdiperstat have been extensively characterized.

Verdiperstat effectively inhibits MPO in vivo and is efficacious in two different MSA models suggesting disease modification potential in MSA. The effect on motor performance, as well as the neuroprotective effect of verdiperstat, was evaluated in a mouse model of early MSA. Mice received vehicle or verdiperstat via oral gavage for 28 days. Significant neuroprotection (Figure X) was demonstrated by verdiperstat, with preservation of neurons at the level of substantia nigra pars compacta, striatum, cerebellar cortex, pontine nuclei, and inferior olivary complex, as well as functional recovery (Figure Y) measured by 4 different behavioral tests (motor score, stride length test, open field activity, rearing). The verdiperstat effect was related to suppression of microglial activation without detectable changes in astrogliosis.

Effects on neuroprotection and microglial activation of treatment with verdiperstat after disease onset were evaluated in a mouse model of advanced MSA. Treatment with verdiperstat was initiated after disease onset and continued for 19-20 days. No improvements in behavioral tests or neuroprotection occurred, but a marked reduction in microglial activation in the brain (SNc, pontine nuclei, inferior olives, corpus callosum) was observed.

A comprehensive toxicology data package has been developed on verdiperstat including single dose toxicity, repeat-dose toxicity (including chronic toxicity in rats and dogs), genetic toxicity, reproductive and developmental toxicity, and special toxicity.

Previous Clinical Trials

Seven clinical studies have been completed, all sponsored by AstraZeneca. These studies include one Phase 2b study in subjects with MSA, two Phase 2a studies in subjects with Parkinson's Disease, and four Phase 1 studies in healthy volunteers, that inform PK, metabolic interactions, safety, tolerability and efficacy. A total of 234 subjects have received verdiperstat to date. A total of 167 subjects in Phase 1 and 2 studies have received multiple doses of verdiperstat (D0490C00002, D0490C00003, D0490C00004, D0490C00005, and D0490C00023), ranging from 50 to 600 mg BID for up to 12 weeks and 900 mg BID for 2.5 days. A total of 67 subjects have received single doses of verdiperstat in Phase 1 studies (Studies D0490C00001 and D0490C00012), ranging from 1 to 50 mg. Overall, the PK and safety profile from the Phase 1 studies provided support for the investigation of verdiperstat at doses up to 600 mg BID in Phase 2 studies.

In a Phase 2b study, subjects with MSA were randomized to receive verdiperstat 300 mg BID, verdiperstat 600 mg BID, or placebo for 12 weeks; efficacy assessments were exploratory. The verdiperstat groups exhibited numerical, but not statistically significant, improvements compared to the placebo group that were dose-related, based on changes in the Unified MSA Rating Scale scores from baseline to Week 12. Placebo-treated subjects worsened by 4.6 points, while BHV-3241 treated subjects showed less worsening of 3.7 points at the 300-mg dose and 2.6 points at the 600-mg dose, suggesting a dose-response relationship. Changes on positron emission tomography (PET) imaging with [11C]-PBR28 binding to translocator protein (TSPO), a marker for microglial activation, did not demonstrate statistically different changes between groups. Verdiperstat treatment for 12 weeks (at doses of 300 mg BID and 600 mg BID) showed statistically significant reductions in certain measures of MPO specific activity in plasma. These results support the intended mechanism of action of verdiperstat. Verdiperstat treatment was generally safe and well-tolerated in MSA subjects at doses of 300 mg and 600 mg BID.

Data from two Phase 2a studies in subjects with Parkinson's disease showed reductions in MPO activity for subjects treated with verdiperstat 600 mg BID compared with placebo-treated subjects, offering further support for the mechanism of action of verdiperstat (i.e., reduced microglial activation). The 300-mg BID dose was safe and well tolerated, and the 600-mg BID dose was generally safe and well tolerated in most subjects.

*Our Clinical Program for Verdiperstat for Multiple System Atrophy*

In January 2019, we received a may-proceed letter from the FDA regarding the continued development of verdiperstat in a Phase 3 randomized controlled trial in patients with MSA. The planned study design is a randomized, double-blind, parallel group study. The estimated sample size is approximately 252 patients. The anticipated dose of verdiperstat (based on the Ph2 study) is 600 mg twice daily. The primary outcome measure is expected to be the Unified MSA Rating Scale. We are expecting to start enrollment in the trial in the third quarter of 2019.

*University of Connecticut License Option*

In October 2018, we signed an exclusive, worldwide option and license agreement with the University of Connecticut for the development and commercialization rights to UC1MT, a therapeutic antibody targeting extracellular metallothionein (MT). Extracellular MT has been implicated in the pathogenesis of autoimmune and inflammatory diseases. Under this agreement, we have the option to acquire an exclusive, worldwide license to UC1MT and its underlying patents to develop and commercialize throughout the world in all human indications.

**Kleo Pharmaceuticals, Inc.**

From August 2016 through November 2018, we made several investments to acquire a minority equity interest in Kleo Pharmaceuticals, Inc. ("Kleo") a privately held, development-stage company founded by a professor of chemistry and pharmacology at Yale University that is developing small molecule immunotherapies that emulate biologics to fight cancers and infectious diseases. We have also entered into a consulting agreement with Kleo to assist Kleo with clinical development. To date, no services have been provided under this agreement.

On August 29, 2016, we entered into a stock purchase agreement with Kleo to purchase 3,000,000 shares of Kleo's common stock at an initial closing, with a commitment to purchase an aggregate of 5,500,000 additional shares of common stock, in each case at a share price of $1.00 per share. We purchased 3,000,000 shares upon the initial closing on August 31, 2016, and the remaining 5,500,000 shares were purchased in four equal tranches of 1,375,000 shares, which we completed in March, June and October 2017, and January 2018. In connection with the initial investment, we received the right to designate two members of Kleo's board of directors.

In March 2017, we purchased 500,000 shares of Kleo common stock directly from a co-founder of Kleo for consideration of $249,750 in cash and 32,500 shares of our common shares.

In addition to these purchases, in October 2017, we purchased an additional aggregate of 2,049,543 shares for cash consideration of $2.3 million and in November 2018 we participated in Kleo's Series B funding raise where we purchased 1,420,818 common shares for cash consideration of $5.0 million. As of the close of the Series B funding raise, and December 31, 2018, our ownership interest in the outstanding stock of Kleo was 41.9%. The Company assigned its shares and the rights under the related agreements to Biohaven Therapeutics Ltd. its wholly owned subsidiary on November 12, 2018.

**Competition**

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary drugs. While we believe that our knowledge, experience and scientific resources provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their safety, efficacy, convenience, price, the level of generic competition and the availability of coverage and reimbursement from government and other third-party payors.

Many of the companies against which we are competing, or against which we may compete in the future, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through

collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

***CGRP Receptor Antagonist Platform***

With regard to rimegepant and BHV-3500, our compounds target acute treatment of migraine and migraine prevention. We face competition from companies that develop and/or sell the following types of migraine treatments:

*Triptans (Acute Treatment of Migraine)*

Clinicians use a number of pharmacologic agents for the acute treatment and/or prevention of migraine. Initial management is often with over-the-counter products (e.g. Excedrin, ibuprofen) or some prescription non-steroidal anti-inflammatories (e.g. diclofenac). The dominant class of prescription medication for the acute treatment of migraine are serotonin 5-HT1B/1D receptor agonists, or triptans. There are seven different triptans (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan), the first of which was developed and approved over 25 years ago and, today, all triptans are generic. The initial introduction of triptans represented a shift toward drugs more selectively targeting the suspected pathophysiology of migraine. A 5-HT1F receptor antagonist, lasmiditan, could be approved as early as 2019. Lasmiditan was developed by CoLucid and acquired by Eli Lilly in January 2017. Lasmiditan could be the first new class of agent approved for the acute treatment of migraine since the triptans and, if approved, would be launched prior to rimegepant. Lasmiditan was designed to act through non-vasoconstrictive mechanisms in the 5-HT1 pathways such that patients who have cardiovascular risk factors, stable cardiovascular disease, or those who are dissatisfied with current triptan therapies could be treated. In August 2017, Lilly announced that lasmiditan met both its primary (pain freedom) and key secondary (most bothersome symptom) endpoints at 2 hours. In November 2018, Lilly announced NDA submission of lasmiditan for the acute treatment of migraine. Preliminary data from lasmiditan, compared with the results from the rimegepant program, would suggest ability to differentiate on both durability of benefit and AEs.

*Other Oral CGRP Candidates in Development*

Since we will be pursuing approval of our orally available, small molecule rimegepant for the acute treatment of migraine, the most relevant comparator to rimegepant is the oral CGRP receptor antagonist under development from Allergan, ubrogepant. Allergan presented results from both of their Phase 3 studies (Achieve 1 annd Achieve 2) in 1H18. on These trials compared different doses (25, 50 and 100mg ) an earnings call from the first of their Phase 3 studies (Achieve 1). These studies evaluated the safety and efficacy of orally administered ubrogepant 25, 50 mg and 100 mg compared to placebo in a single migraine. The 50 and 100mg doses showed a statistically greater percentage of ubrogepant patients pain free at 2 hours as compared to placebo, as well as statistical significance on the co-primary, absence of the most bothersome migraine associated symptom at 2 hours post dose. Patients were permitted to take a second dose of investigational product or rescue medication after the 2 hour time point. Durability of effect at 24 hours was not achieved with all doses (only the 100mg dose demonstrated 24-hour sustained pain relief). Ubrogepant was well tolerated with an adverse event profile similar to placebo. There were 6 cases of LFTs (ALT or AST) >3x ULN (1 on placebo, 5 on ubrogepant): 2 cases of LFTs >5x ULN on ubrogepant and 1 case of LFTs >10x ULN on ubrogepant in Achieve 1 and 4 cases of LFTs (ALT or AST) >3x ULN (1 on placebo and 3 on ubrogepant 50mg). No cases were determined to have a probable relationship to study drug. There were no cases of Hy's Law. Launch of ubrogepant is anticipated in the first quarter 2020. Based on the published Phase 2 studies with both of rimegepant and ubrogepant, and the data presented to date from the Phase 3 studies of ubrogepant, we believe rimegepant has the potential to be best-in-class. Allergan is a global pharmaceutical company with presence in the CNS area and, in particular, with physicians treating chronic migraine through its Botox franchise.

*Other Acute Treatments for Migraine*

Ergot alkaloids (such as Dihydroergotamine ("DHE")), analgesics, including opioids, NSAIDs, acetaminophen and antiemetics also are used in the acute treatment of migraine. DHE is also a potent vasoconstrictor and has been primarily displaced by the introduction of the triptans. Opioid use for migraine is associated with increased disability and health care utilization. Opioids, while effective for headache pain, are not approved for migraine and carry risk of abuse and addiction.

*Migraine Prevention Treatments*

Agents currently used to reduce the frequency of migraine episodes were first approved for other uses (e.g. beta blockers, antidepressants, anticonvulsants). Botox is the only product that has been approved by the FDA for the prevention of chronic migraine (defined as at least 15 headache days per month, at least 8 of which are migraine). For those patients who do not qualify as having chronic migraine, but still have significant disability due to migraine, there are five products approved by the FDA for use: topiramate (Topamax) and valproic acid (Depakote), both anticonvulsant medicines, propranolol (Inderal) and timolol (Blocadren), both beta-blockers, and amitriptyline, a tricyclic antidepressant.

The biologic CGRP therapies have been studied for the prevention of migraine with three agents approved in 2018. . The three new FDA-approved drugs, Aimovig (erenumab-aooe), Ajovy (fremanezumab-vfrm), and Emgality (galcanezumab-gnlm), are all administered subcutaneously.These therapies, while effective, do not eliminate the need for acute treatment of migraine attacks. In addition, they all require SQ administration. We believe that BHV-3500 may have the opportunity to differentiate from these therapies due to its potential to be used for both the acute treatment and prevention of migraine.

***Glutamate Platform***

With respect to troriluzole, which we are currently developing for the treatment of ataxias, OCD, Alzheimer's disease, and GAD, there are currently no approved drug treatments for SCA or any other cerebellar ataxia, in the United States.

We are aware of companies with clinical stage programs in development for potential treatments for SCA and other cerebellar disorders, including Bioblast Pharma, which is in Phase 2 development of trehalose, which targets SCA 3 and acts as a protein stabilizer; Steminent Biotherapeutics, which is currently conducting a Phase 2 trial of allogeneic adipose-derived mesenchymal stem cells that target polyglutamine SCAs; EryDel which is planning a Phase 3 trial for its product, IEDAT01, which delivers dexamethasone sodium phosphate through red blood cells, Shionogi & CO., Ltd., which is investigating Rovatirelin, a non-peptide mimetic of thyrotropin-releasing hormone, in a Phase 3 trial in Japan; Shire Plc, which is exploring Cuvitru, an intravenous immune globulin that is approved for the treatment of primary immunodeficiency disorders, in Phase 2 development. Mitsubishi Tanabe received approval for taltirelin, an oral thyrotropin releasing hormone, in Japan in 2009 but has not filed with the FDA to seek approval in the United States.

With regards to OCD, there have been no new classes of drugs approved in over a decade. We are not aware of other product candidates besides troriluzole that are currently in clinical development targeting populations with OCD.

With respect to BHV-0223, which we are developing for the treatment of ALS, we believe our primary competitor is Covis Pharmaceuticals, which sells Rilutek, the brand name for riluzole. Riluzole is also generically available. Edaravone (Radicava, Mitsubishi Tanabe Pharma) was recently approved by the FDA in May 2017 for the treatment of ALS, based on efficacy studies conducted in Japan with the vast majority of patients on background riluzole therapy. Edaravone is administered to patients by intravenous infusion. We are aware of at least two other companies that are marketing or plan to market new formulations of riluzole: Aquestive Therapeutics has publicly announced they plan to file an NDA for a riluzole oral soluble film in 2019, and Italfarmaco SpA, a private Italian company, markets an oral liquid suspension formulation of riluzole in the United Kingdom and elsewhere in Europe under the brand name Tiglutik. Tiglutik, the US brand name for Italfarmaco's oral liquid suspension formulation of riluzole was approved for marketing in the United States in September 2018. Being that an oral suspension still requires swallowing in a population prone to dysphagia, we believe an oral dissolvable tablet that may not require swallowing will have significant market preference. We are aware of several companies that are exploring potential treatments for ALS, mostly agents with novel mechanisms of action being administered with riluzole. We are not aware of any company marketing or developing a sublingual formulation of riluzole. Other companies of which we are not aware may also be developing formulations using the API riluzole; if such companies pursued regulatory approval of such product candidates using the Section 505(b)(2) regulatory pathway, those product candidates would potentially compete with BHV-0223. For example, Italfarmaco and Aquestive have obtained orphan designation for their products, and are eligible to obtain orphan exclusivity subject to a showing of clinical superiority to riluzole. Based on orphan drug designation requirements, the first approval of a novel formulation of riluzole may obligate subsequent formulations to demonstrate advantages with regard to safety, efficacy or meaningful contribution to patient care, in order to achieve marketing authorization.

With respect to BHV-5000, which we are developing for the treatment of Rett syndrome, there are currently no approved treatments for Rett syndrome in the United States. We are aware of companies with clinical stage programs in development for potential treatments for Rett syndrome, including Newron Pharmaceuticals SpA which is launching a Phase 2/3 clinical trial of sarizotan, an agent with serotonin subtype-1A (5-HT1A) receptor agonist and dopamine subtype-2 (D2) receptor antagonist activities, and Neuren Pharma, which has completed a Phase 2a trial of trofinetide in adult patients and a Phase 2 trial in pediatric patients with Rett syndrome.

If we expand our development of troriluzole, BHV-0223 or BHV-5000 into additional neuropsychiatric or other indications, we would face substantial competition from companies that develop or sell products that treat those indications.

***Other Platforms***

With respect to verdiperstat, which we are developing for the treatment of MSA, there are currently no approved treatments for MSA in the United States. We are not aware of any planned or ongoing late stage development programs for

MSA. Nevertheless, we are aware of companies who have, at some time, declared that they are developing potential treatments for MSA, including the following:

- Prana Biotechnology Ltd, PBT434 is a small molecule purported to inhibit the aggregation of α-synuclein and tau that was granted orphan drug designation in the US in January 2019;
- AFFiRiS AG;
- Corestem Inc;
- MitoDys Therapeutics Ltd;
- Modag GmbH; and
- Neuropore Therapies Inc.

**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 preclinical and clinical testing, as well as for commercial manufacturing if our product candidates receive marketing approval.

Our lead product candidates are small molecules and 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 intend to develop and, if approved by the FDA, commercialize our product candidates in the United States, and we may enter into distribution or licensing arrangements for commercialization rights for other regions.

With respect to rimegepant and BHV-3500, we plan to build a specialty team of sales and medical marketing professionals to focus on targeting neurological specialists and headache centers in the United States, potentially in combination with a larger pharmaceutical partner, to maximize patient coverage in the United States and to support global expansion.

With respect to the product candidates in our glutamate modulation and MPO platforms, we currently intend to build a neurological specialty sales force to manage commercialization for these product candidates on our own.

**Intellectual Property**

We strive to protect and enhance the proprietary technologies that we believe are important to our business, including seeking and maintaining patents intended to cover our products and compositions, their methods of use and any other inventions that are important to the development of our business. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business, defend and enforce our patents, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain the proprietary position of our products and our other development programs.

***Patents and Patent Applications***

We have approximately 500 U.S. and foreign patents and patent applications in our portfolio related to the composition of matter, methods of use, methods of manufacture or formulations of our product candidates which have been filed in major markets throughout the world, including the United States, Europe, Japan, Korea, China, Hong Kong and Australia. About 1/3 of the patents and patent applications support the Glutamate platform and 2/3 supports the CGRP platform.

*Rimegepant and BHV-3500*

The intellectual property rights related to rimegepant and BHV-3500 are in-licensed from BMS and are covered by five families of U.S. and certain selected foreign patents, with statutory expiration dates ranging from 2023 to 2033. U.S. Patent 8,314,117 covers the composition of matter of rimegepant, and has a statutory expiration date of October 12, 2030, not including patent term adjustment or any potential patent term extension. U.S. Patent 8,481,546 covers the composition of matter of BHV-3500, and has a statutory expiration date of March 2, 2031, not including patent term adjustment or any potential patent term extension. These or other patents cover rimegepant and BHV-3500 and their use in treating migraine and, in certain ex-U.S. jurisdictions, other neurological conditions. The license also includes several patent families of related compounds directed to the CGRP receptor. We also have an agreement with Catalent whereby Catalent granted an exclusive license under certain of its patents and technology to use the Zydis ODT technology for development of our rimegepant product. Catalent retains all manufacturing rights.

*Troriluzole*

We own several families of patent applications containing claims directed to prodrugs of riluzole. These patent applications include several U.S. applications and corresponding PCT applications. These families of patent applications contain claims directed to troriluzole and numerous other prodrugs of riluzole. In addition, the use of these compounds for treating ALS, SCA, depression and other diseases is described and claimed in these patent applications. We own these patent applications subject to a license agreement with ALS Biopharma and Fox Chase Chemical Diversity Center, Inc. If a patent covering troriluzole issues from one of these pending patent application families, it would have a statutory expiration date in 2036. Other patent applications provide coverage for alternative formulations of riluzole prodrugs and their uses.

*BHV-0223*

BHV-0223, a sublingual or ODT form of riluzole, and its use for treating various forms of pain, ALS and depression are covered by patent applications pending in the U.S. and selected foreign jurisdictions having a statutory expiration date in 2035. We have an agreement with Catalent whereby Catalent granted an exclusive license under certain of its patents and technology to use the Zydis ODT technology for our BHV-0223 product. Catalent retains all manufacturing rights. In addition to patent protection, although not an NCE, BHV-0223 may also be entitled to certain regulatory exclusivity. In addition to the patent applications we own, we have also licensed one issued patent and several pending patent applications from Yale University which provide protection for the use of riluzole in treating generalized anxiety disorder and other neurological uses, respectively. Further, we have licensed several patents from Rutgers University covering the use of riluzole for treating various forms of cancer and an animal model for tumors which may cover the use of BHV-0223 for treating the specific cancers.

*BHV-5000*

We have also in-licensed one patent family related to certain uses of lanicemine and a patent application family containing claims directed to BHV-5000 from AstraZeneca. They contain claims directed to the use of the base compound, lanicemine, in treating depression, and the structure of the prodrug form, BHV-5000, as well as the use of the prodrug in treating a variety of neurological diseases including Rett syndrome and depression. The issued patents related to uses of lanicemine have a statutory expiration date in 2020. Two U.S. patents have been granted that are directed to BHV-5000 and its uses and have a statutory expiration date in 2034. Corresponding foreign patents are pending.

*Verdiperstat*

In September 2018, we in-licensed a patents from AstraZeneca relating to the composition of matter of verdiperstat, pharmaceutical compositions and various neurological diseases including muscular system atrophy. The patent applications have been filed in the U.S., Europe, Japan and other countries. Three U.S. patents have been granted. The pending applications and granted patents have expiration dates from 2025 to 2034, not including possible patent term extensions.

*Additional Licensed Patent Applications*

We have also licensed a family of patent applications related to the treatment of depression with a combination of ketamine and scopolamine from Massachusetts General Hospital.

*Patent Protection and Terms*

The term of individual patents depends on the legal term for patents in the countries in which they are granted. In most countries, including the United States, the patent term is generally 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable country. In the United States, a patent's term may, in certain cases, be extended by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over a commonly owned patent or a patent naming a common inventor and having an earlier expiration date. The Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Act") permits a patent term extension of up to five years beyond the expiration date of a U.S. patent as partial compensation for the length of time the drug is under regulatory review. Patent term extension is not available for all approved products and, even if an approved product is eligible, only one patent covering the approved product may be extended, the extension can only be based on a single approved product, and the total extension granted cannot extend the remaining term of the patent beyond 14 years from product approval.

Furthermore, the patent positions of biotechnology and pharmaceutical products and processes like those we intend to develop and commercialize are generally uncertain and involve complex legal and factual questions. No consistent policy regarding the breadth of claims allowed in such patents has emerged to date in the United States. The patent situation outside the United States is even more uncertain. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries can diminish our ability to protect our inventions and enforce our intellectual property rights, can make it easier to challenge the validity, enforceability or scope of any patents that may issue, and, more generally, could affect

the value of intellectual property. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents.

***Third-Party Patent Filings***

Numerous U.S. and foreign issued patents and patent applications owned by third parties exist in the fields in which we are developing products. In addition, because patent applications can take many years to issue, there may be applications unknown to us, which may later result in issued patents that our product candidates or proprietary technologies may infringe. Moreover, we may be aware of patent applications, but incorrectly predict the likelihood of those applications issuing with claims of relevance to us.

Under U.S. law, a person may be able to patent a discovery of a new way to use a previously known compound, even if such compound itself is patented, provided the newly discovered use is novel and non-obvious. Such a method-of-use patent, however, if valid, only protects the use of a claimed compound for the specified methods claimed in the patent. This type of patent does not prevent persons from using the compound for any previously known use of the compound. Further, this type of patent does not prevent persons from making and marketing the compound for an indication that is outside the scope of the patented method.

***License Agreements***

*License Agreement with BMS*

*Overview*

In July 2016, we entered into an exclusive, worldwide license agreement with BMS for the development and commercialization rights to rimegepant and BHV-3500, as well as other CGRP-related intellectual property. Subject to certain limitations and certain retained rights of BMS, the license included an exclusive license under certain BMS patent rights and BMS know-how to the extent necessary to research, discover, develop, make, have made, use, sell, offer to sell, export and import licensed compounds and licensed products in the field of prevention, treatment or control of any disease, disorder or condition in humans. In exchange for these rights, we agreed to pay BMS initial payments, milestone payments and tiered royalties on net sales of licensed products under the agreement. Our initial payments to BMS totaled $9.0 million and were paid within 90 days after entering into the agreement. The milestone payments due to BMS under the agreement consist of development and commercial milestones. The development milestones due under the agreement depend on the licensed product being developed. Development milestones due under the agreement with respect to rimegepant or a derivative thereof total up to $127.5 million, and, for any product other than rimegepant or a derivative thereof, total up to $74.5 million. Commercial milestones total up to $150.0 million for each licensed product. If we receive revenue from sublicensing any of our rights under the agreement, we are also obligated to pay a portion of that revenue to BMS as well. The tiered royalty payments are based on annual worldwide net sales of licensed products under the agreement, with percentages in the low-to-mid teens.

We made a payment of $5.0 million to BMS pursuant to our obligations under the BMS agreement during the third quarter of 2017 for the achievement of a specified milestone.

*Our Development, Regulatory and Commercialization Obligations*

Under the agreement, we are obligated to use commercially reasonable efforts to develop licensed products using the patent rights we have licensed from BMS, including setting forth a development plan with specific development activities and timelines, updating the development plan each year, providing BMS with annual reports of our progress and keeping BMS informed of material changes that may affect the development plan. With respect to any of the licensed products, we are solely responsible for all development, regulatory and commercial activities and costs. We are also obligated to use commercially reasonable efforts to achieve specified regulatory and commercial milestones, and maintain a sufficient supply of our products to satisfy our expected commercialization efforts in each country in which we sell such products. Following our first commercial sale of a product, we must provide BMS with periodic reports of our commercial activities. In connection with the agreement, BMS agreed to use commercially reasonable efforts to assign and transfer any INDs for the licensed compounds to us.

*Equity Consideration*

As part of the agreement, we agreed to issue BMS common shares in the amount of $12.5 million upon the occurrence of specified events, including upon an initial public offering ("IPO"). In satisfaction of this obligation, in May 2017 upon the completion of our IPO, we issued 1,345,374 common shares to BMS.

*Non-Competition*

Until 2023, neither we nor our affiliates may, ourselves or through or in collaboration with a third party, engage directly or indirectly in the clinical development or commercialization of specified competitive compounds. In the event that we are or become non-compliant with this provision due to licensing, collaboration or acquisition activity, we must either divest ourselves of the competitive compound within a certain period of time, discontinue the development of the competitive compound, or negotiate with BMS to have the competitive compound included as a licensed product under our agreement with BMS. The failure to so divest or reach terms with BMS may result in the termination of our license with BMS.

*Term and Termination*

The agreement will terminate on a licensed product-by-licensed product and country-by-country basis upon the expiration of the royalty term with respect to each licensed product in each country. The patents related to the licensed products have statutory expiration dates ranging from 2023 to 2033.

BMS has the right to terminate the agreement upon our insolvency or bankruptcy, our uncured material breach, including our failure to meet our development and commercialization obligations, our challenge to any BMS patent rights, or our failure to close a financing within specified parameters. We have the right to terminate the agreement if BMS materially breaches the agreement or if, after we provide notice, we choose not to move forward with development and commercialization in a specific country. In the event that BMS exercises its right to terminate the agreement following our insolvency, our breach of the agreement or our failure to develop or commercialize the licensed compounds, or if we terminate the agreement after providing notice, all rights and licenses granted to us will terminate, and all patent rights and know-how transferred pursuant to the agreement will revert to BMS. In addition, upon such termination, we agree to, at BMS's election, (i) assign all regulatory filings, approvals and regulatory documents necessary to further develop and commercialize the reverted products or (ii) withdraw or inactivate such filings and approvals.

*Amendment to License Agreement with Bristol-Myers Squibb Company*

In March 2018, the Company entered into an Amendment to License Agreement (the “BMS Amendment”) with BMS, which amends the License Agreement between the Company and BMS from July 2016 (the “Original License Agreement” and, as amended by the BMS Amendment, the “BMS License Agreement”). Under the BMS Amendment, the Company paid BMS an upfront payment of $50.0 million in return for a low single-digit reduction in the royalties payable on net sales of rimegepant and a mid single-digit reduction in the royalties payable on net sales of BHV-3500, recorded in Research and Development expense in the Consolidated Statements of Operations and Comprehensive Loss. Under the Original License Agreement, the Company was obligated to make tiered royalty payments based on annual worldwide net sales of licensed products upon their approval and commercialization, with percentages in the low- to mid-teens.

The BMS Amendment also removes BMS’s right of first negotiation to regain its intellectual property rights or enter into a license agreement with the Company following the Company’s receipt of topline data from its Phase 3 clinical trials with rimegepant, and clarifies that antibodies targeting CGRP are not prohibited as competitive compounds under the non-competition clause of the Original License Agreement.

The BMS License Agreement continues to provide the Company with exclusive global development and commercialization rights to rimegepant, BHV-3500 and related CGRP molecules, as well as related know-how and intellectual property. The Company’s obligations to make development and commercial milestone payments to BMS under the Original License Agreement remain unchanged.

*Agreement with ALS Biopharma, LLC and Fox Chase Chemical Diversity Center Inc.*

In August 2015, we entered into an agreement with ALS Biopharma and Fox Chase Chemical Diversity Center, Inc. ("FCCDC") pursuant to which ALS Biopharma and FCCDC assigned to us their worldwide patent rights to a family of over 300 prodrugs of glutamate modulating agents, including troriluzole, as well as other innovative technologies. In addition, we received a non-exclusive license to certain trade secrets and know-how of ALS Biopharma. We took assignment of these patent rights subject to the provisions of the Bayh Dole Act, as applicable, to the extent that any invention included with the assigned patent rights was funded in whole or in part by the United States government. In addition, certain of the patent rights that do not cover troriluzole were co-owned by Rutgers, and thus, we took assignment of these patent rights subject to the co-ownership interest of Rutgers. Under the agreement, we are obligated to use commercially reasonable efforts to diligently commercialize and develop markets for the patent products.

As consideration for this assignment of patent rights, we paid ALS Biopharma $2.5 million between August 2015 and November 2016 as funding for research to be performed by ALS Biopharma in connection with a mutually agreed upon research plan. We are also obligated to pay regulatory milestone payments of $3.0 million upon a specified regulatory approval for the first licensed product under the agreement as well as additional milestone payments of $1.0 million for each licensed

product that completes the specified regulatory milestone thereafter. We are also obligated to make royalty payments of a low single-digit percentage based on net sales of products licensed under the agreement, payable on a quarterly basis.

*Equity Consideration*

As part of the agreement, we also issued to ALS Biopharma 50,000 common shares as well as two warrants to purchase a total of 600,000 common shares with an exercise price of $5.60 per share, of which 275,000 shares were immediately exercisable at issuance and the remaining 325,000 shares became exercisable upon our achievement of a specified regulatory milestone. This milestone was achieved in May 2016. We also agreed to grant specified preemptive rights to ALS Biopharma to participate in equity offerings that are open to our other shareholders.

In January 2018, ALS Biopharma exercised a warrant for the purchase of 275,000 shares through a net share settlement. The Company issued 228,119 shares as a result of the exercise.

*Term and Termination*

The agreement terminates on a country-by-country basis as the last patent rights expire in each such country. Our current patent rights consist of owning several families of patent applications. If a patent covering troriluzole issues from one of these pending patent applications, it would have a statutory expiration date in 2036. ALS Biopharma has the right to terminate the agreement or its applicability to one or more countries upon 30 days' prior written notice to us if we fail to make an undisputed payment within the 60-day period after receipt of a termination notice or if we commit a material breach of the agreement that is not cured within the 60-day period after receipt of a termination notice. We have the right to terminate the agreement if ALS Biopharma commits a material breach of the agreement that is not cured within the 60-day period after written notice thereof from us or, as to a specific country, if no valid claims exist in such country. Both we and ALS Biopharma may terminate the agreement as to a specific country if we are enjoined from exercising our patent rights under the agreement in such country. If we affirmatively abandon our development, research, licensing or sale of all products covered by one or more claims of any patent or patent application assigned under the agreement, or if we cease operations, we have agreed to reassign the applicable patent rights back to ALS Biopharma.

*2016 License Agreement with AstraZeneca*

*Overview*

In October 2016, we entered into an exclusive license agreement with AstraZeneca, or the 2016 AstraZeneca Agreement, pursuant to which AstraZeneca granted us a license to certain patent rights and know-how for all human uses for the commercial development, manufacture, distribution and use of any products or processes resulting from development of those patent rights, including BHV-5000 and lanicemine.

Under the 2016 AstraZeneca Agreement, we have the right to sublicense our rights under the agreement subject to AstraZeneca's prior written consent, such consent not to be unreasonably withheld, conditioned or delayed. We will be responsible for preparing, filing, prosecuting and maintaining the licensed patents and applications, and for Orange Book listing any listable patents. We have the right to enforce the licensed patents and to defend challenges to the validity or enforceability of the licensed patents. AstraZeneca, however, retains the right to apply for patent term extensions for the licensed patents. We may not assign our rights or delegate our obligations under the 2016 AstraZeneca Agreement without AstraZeneca's consent, including in the event of a change of control.

In exchange for these rights, in addition to the agreement to issue equity consideration noted below, we agreed to pay AstraZeneca an upfront payment, milestone payments and royalties on net sales of licensed products under the agreement. We made the upfront payment to AstraZeneca of $5.0 million upon signing the agreement. The milestone payments due to AstraZeneca under the agreement consist of regulatory and commercial milestones. The regulatory milestones due under the agreement depend on the indication of the licensed product being developed as well as the territory where regulatory approval is obtained. Development milestones due under the agreement with respect to Rett syndrome total up to $30.0 million, and, for any indication other than Rett syndrome, total up to $60.0 million. Commercial milestones are based on net sales of all products licensed under the agreement and total up to $120.0 million. We have agreed to pay tiered royalties of mid single-digit to low double-digit percentages based on net sales of products licensed under the agreement. If we receive revenue from sublicensing any of our rights under the agreement, we are also obligated to pay a portion of that revenue to AstraZeneca.

*Our Development, Regulatory and Commercialization Obligations*

Under the agreement, we are obligated to use commercially reasonable efforts to develop, and obtain and maintain regulatory approvals for, licensed products using the rights we have licensed from AstraZeneca, including providing AstraZeneca with annual reports of our development activities. With respect to any of the licensed products, we are solely responsible for all development, regulatory and commercial activities and costs. Following our first commercial sale of a

product, we must provide AstraZeneca with periodic reports of our commercial activities. AstraZeneca agreed to use commercially reasonable efforts to transfer all of its regulatory documentation related to BHV-5000 and lanicemine in each country to us, including all INDs, NDAs and approvals, promptly following the effective date of the agreement.

*Right of First Negotiation*

After we receive topline data from the first Phase 2b study of a product candidate licensed under the agreement, we must provide notice and a summary of the data to AstraZeneca. AstraZeneca will then have a period of time to exercise its right of first negotiation to regain its intellectual property rights or enter into a sublicense agreement with us. If AstraZeneca does not give notice of its intent to exercise its right of first negotiation during this time period, or we do not execute a definitive agreement within an additional time period, we will have the sole right, in our discretion, to negotiate and execute any agreement with third parties, or to retain our rights.

*Equity Consideration*

As part of the consideration, we agreed to issue to AstraZeneca common shares in the amount of $5.0 million if we completed a financing within specified parameters. This condition was satisfied upon the closing of our Series A preferred share financing, at which time we issued 538,150 Series A preferred shares to AstraZeneca which, at the completion of our IPO, automatically converted into 538,150 common shares. In addition, we agreed to issue to AstraZeneca common shares in the amount of $5.0 million upon the completion of specified events, including upon an IPO. In satisfaction of this obligation, in May 2017 upon the completion of our IPO, we issued an additional 538,149 common shares to AstraZeneca.

*Term and Termination*

The 2016 AstraZeneca Areement will terminate upon the expiration of the last royalty term for the last licensed product under the agreement. Each royalty term begins on the date of the first commercial sale of the applicable licensed product in the applicable country and ends on the later of 10 years from such first commercial sale or the expiration of the last to expire of the applicable patents in that country. The patent applications related to BHV-5000 would, if issued, have a statutory expiration date in 2033. Either party may terminate the agreement upon the other party's uncured material breach or upon insolvency or bankruptcy. AstraZeneca also has the right to terminate the agreement in certain circumstances. We have the right to terminate the agreement without cause. In the event the agreement is terminated in its entirety for any reason, all rights and licenses granted to us by AstraZeneca under the agreement, and all sublicenses granted by us under the agreement, immediately terminate, and we are required to assign to AstraZeneca all of the regulatory documentation applicable to any licensed compound or licensed product owned or controlled by us or our affiliates, to transfer control of any clinical studies involving licensed products to AstraZeneca and continue such studies at our cost for six months, and to assign to AstraZeneca all of our agreements with third parties that are reasonably necessary for the exploitation of the licensed products.

*2018 License Agreement with AstraZeneca*

*Overview*

In September 2018, we entered into an exclusive license agreement with AstraZeneca, or the 2018 AstraZeneca Agreement, pursuant to which AstraZeneca granted us exclusive worldwide rights to develop and commercialize verdiperstat. In exchange for these rights, we paid AstraZeneca an upfront cash payment of $3.0 million and issued AstraZeneca 109,523 common shares, valued at $4.1 million on the date of settlement. We are obligated to pay milestone payments to AstraZeneca totaling up to $55.0 million upon the achievement of specified regulatory and commercial milestones and up to $50.0 upon the achievement of specified sales-based milestones. In addition, we will pay AstraZeneca tiered royalties ranging from high single-digit to low double-digits based on net sales of specified approved products, subject to specified reductions.

We may sublicense our rights under the 2018 AstraZeneca Agreement and, if we do so, we will be obligated to pay a portion of any milestone payments received from the sublicensee to AstraZeneca in addition to any milestone payments we would otherwise be obligated to pay.

*Our Development, Regulatory and Commercialization Obligations*

Under the 2018 AstraZeneca Agreement, we are solely responsible, and have agreed to use commercially reasonable efforts, for all development, regulatory and commercial activities related to verdiperstat. We are also responsible for the prosecution and maintenance of the patents related to verdiperstat and have the first right to prosecute infringement of the patents and defend challenges to the validity or enforceability of the patents.

*Term and Termination*

The 2018 AstraZeneca Agreement terminates on a country-by-country basis and product-by-product basis upon the expiration of the royalty term for such product in such country. Each royalty term begins on the date of the first commercial sale

of the licensed product in the applicable country and ends on the later of 10 years from such first commercial sale or the expiration of the last to expire of the applicable patents in that country. The 2018 AstraZeneca Agreement may be terminated earlier in specified situations, including termination for uncured material breach of the 2018 AstraZeneca Agreement by either party, termination by AstraZeneca in specified circumstances, termination by us on a country-by-country basis with advance notice and termination upon a party's insolvency or bankruptcy.

*Agreements with Catalent U.K. Swindon Zydis Limited*

In March 2015, we entered into a development and license agreement with Catalent pursuant to which we obtained certain license rights to the Zydis ODT technology in BHV-0223. BHV-0223 was developed under this agreement. Catalent has manufactured BHV-0223 for clinical testing and we expect them to do so for commercial supply. We made an upfront payment of $0.3 million to Catalent upon entering into the agreement and are obligated to pay Catalent up to $1.6 million upon the achievement of specified regulatory and commercial milestones. We are also obligated to make royalty payments of a low single-digit percentage based on net sales of products licensed under the agreement.

Under the agreement, we are responsible for conducting clinical trials and for preparing and filing regulatory submissions. We have the right to sublicense our rights under the agreement subject to Catalent's prior written consent. Catalent has the right to enforce the patents covering the Zydis technology and to defend any allegation that a formulation using Zydis technology, such as BHV-0223, infringes a third party's patent.

The development and license agreement terminates on a country-by-country basis upon the later of (i) 10 years after the launch of the most recently launched product in such country and (ii) the expiration of the last valid claim covering each product in such country, unless earlier voluntarily terminated by us. Our current patent rights with respect to BHV-0223 consist of owning several patent applications. If a patent covering BHV-0223 issues from one of these pending patent applications, it would have a statutory expiration date in 2035. The agreement automatically extends for one-year terms unless either party gives advance notice of intent to terminate. In addition, Catalent may terminate the agreement either in its entirety or terminate the exclusive nature of the agreement on a country-by-country basis if we fail to meet specified development timelines, which we may extend in certain circumstances.

In January 2018, we entered into a development and license agreement with Catalent pursuant to which we obtained certain license rights to the Zydis ODT technology for use with rimegepant. If we obtain regulatory approval or launch a rimegepant product that utilizes the Zydis ODT technology, we are obligated to pay Catalent up to $1.5 million upon the achievement of specified regulatory and commercial milestones. If we commercialize a rimegepant product that utilizes the Zydis ODT technology, the agreement permits us to purchase the commercial product from Catalent at a fixed price, inclusive of a royalty. Under the agreement, Catalent agreed that it will not develop or manufacture a formulation of any oral CGRP compound using Zydis ODT technology for itself or a third party for a specified period of time, subject to certain minimum commercial revenues.

In July 2018, we entered into a commercial supply agreement with Catalent pursuant to which Catalent will exclusively manufacture and supply our worldwide requirements for rimegepant in the Zydis ODT delivery formulation, if we pursue and receive regulatory approval of this formulation of rimegepant, for an initial term of five years after its commercial launch with optional two-year renewal periods. Under the agreement, Catalent will supply the rimegepant Zydis ODT product at a fixed price, inclusive of a royalty, and will not develop or manufacture a formulation of any oral CGRP compound using Zydis ODT technology for itself or a third party for a specified period of time, subject to certain minimum commercial revenues.

*License Agreement with Yale University*

In September 2013, we entered into an exclusive license agreement with Yale to obtain rights under certain patent rights for the commercial development, manufacture, distribution, use and sale of products and processes resulting from the development of those patent rights related to the use of riluzole in treating various neurological conditions such as general anxiety disorder, post-traumatic stress disorder and depression. As part of the consideration for this license, we issued Yale 250,000 of our common shares and granted Yale the right to purchase up to 10% of the securities issued in each of our equity offerings. Under the terms of the agreement, in the event of a change of control, as defined in the agreement to include our IPO, we will be obligated to pay to Yale the lesser of (i) 5% of the dollar value of all initial and future potential consideration paid or payable by the acquirer or (ii) $1.5 million as a change-of-control payment. In the event of an IPO, which we completed in May 2017, the change-of-control payment to Yale is reduced by the value of Yale's equity investment in our company. The value of this change-of-control payment was determined to be zero at the expiration of the lockup period in October 2017 since the value of shares at the end of the lockup were worth more than their initial equity investment.

In addition, we agreed to pay Yale regulatory milestone payments of up to $2.0 million and annual royalty payments of a low-single digit percentage based on net sales of products from the licensed patents, subject to a minimum amount of up to

$1.0 million per year. If we grant any sublicense rights under the agreement, we must pay Yale a low single-digit percentage of sublicense income that we receive.

The agreement also requires us to meet certain due diligence requirements based upon specified milestones. We can elect to extend the due diligence requirements by a maximum of one year upon payments of up to $150,000 to Yale. We are also required to reimburse Yale for any fees that Yale incurs related to the filing, prosecution, defending and maintenance of patent rights licensed under the agreement. In the event that we fail to make any payments, commit a material breach, fail to maintain adequate insurance or if we challenge the patent rights of Yale, Yale can terminate the agreement. We can terminate the agreement with 90-days' notice if Yale commits a material breach or in a specific country if there are no valid patent rights. The agreement expires on a country-by-country basis upon the later of expiration of the patent rights or ten years from the date of first sale. Any patent that has issued or does issue from one of the pending patent applications under this agreement would have a statutory expiration date in 2026.

*License Agreement with The General Hospital Corporation d/b/a Massachusetts General Hospital*

In September 2014, we entered into a license agreement with The General Hospital Corporation d/b/a Massachusetts General Hospital ("MGH") pursuant to which MGH granted us a license under certain patent rights for the commercial development, manufacture, distribution and use of any products or processes resulting from development of those patent rights, related to treating depression with a combination of ketamine and scopolamine. Under this agreement, we paid MGH an upfront license fee of $20,000. We are also obligated to pay MGH annual license maintenance fees up to $50,000, beginning in 2017. In addition, we are obligated to pay MGH future milestone payments of up to $750,000 upon the achievement of specified clinical and regulatory milestones and up to $2.5 million upon the achievement of specified commercial milestones. We have also agreed to pay MGH royalties of a low single-digit percentage based on net sales of products licensed under the agreement. We are also required to reimburse MGH for any fees that MGH incurs related to the filing, prosecution, defending and maintenance of patent rights licensed under the agreement. If we receive revenue from sublicensing any of our rights under the agreement, we are also obligated to pay a portion of that revenue to MGH.

The agreement expires upon the expiration of the patent rights licensed under the agreement, which could occur as early as 2033, unless earlier terminated by either party.

*License Agreement with Rutgers, The State University of New Jersey*

In June 2016, we entered into an exclusive license agreement with Rutgers, The State University of New Jersey, licensing several patents and patent applications related to the use of riluzole to treat various cancers. Certain of the Rutgers patent rights were developed using federal funding. Accordingly, the U.S. Government has certain rights in the Rutgers patents and applications. We have the right to sublicense our rights under the Rutgers Agreement. We are responsible for prosecuting and maintaining the patents and applications in the Rutgers patent rights, and Rutgers has an opportunity to review and comment on correspondences with government patent offices. We have the right to prepare any documents related to the application for an extension of the term of any licensed patent and to list any listable patents in the Orange Book. We have the first right to enforce the licensed patents.

Under this agreement, we are required to pay Rutgers annual license maintenance fees of up to $25,000 per year until the first commercial sale of a licensed product. We are also obligated to pay Rutgers payments totaling up to $825,000 upon the achievement of specified clinical and regulatory milestones. We also agreed to pay Rutgers royalties of a low single-digit percentage based on net sales of licensed products sold by us, our affiliates or sublicensees, subject to a minimum of up to $100,000 per year. If we grant any sublicense rights under the license agreement, we must pay Rutgers a low double-digit percentage of sublicense income we receive. In the event that we experience a change of control or sale of substantially all of our assets prior to the initiation of a Phase 3 trial related to products licensed under the agreement, and such change of control or sale results in a full liquidation of our company, we will be obligated to pay Rutgers a change-of-control fee equal to 0.3% of the total value of the transaction, but not less than $100,000.

The agreement also requires us to meet certain due diligence requirements based upon specified milestones. We can elect to extend the due diligence requirements by a maximum of one year upon payments to Rutgers of up to $500,000 in the aggregate.

The agreement expires on a country-by-country basis upon the later of expiration of the last patent rights to expire in such country, which could occur as early as 2024, or ten years from the date of first commercial sale of a licensed product, unless terminated by either party.

*Revenue Participation Right with Royalty Pharma*

In June 2018, pursuant to a Funding Agreement we entered into with Royalty Pharma ("RPI") we granted to RPI the right to receive certain revenue participation payments, subject to certain reductions, based on the future global net sales of the pharmaceutical products containing the compounds rimegepant or BHV-3500 and certain derivative compounds thereof ("Products"), for each calendar quarter during the royalty term contemplated by the Funding Agreement, in exchange for $100.0 million in cash. Specifically, the participation rate commences at 2.1 percent on annual global net sales of up to and equal to $1.5 billion, declining to 1.5 percent on annual global net sales exceeding $1.5 billion.

*Optional License Agreement with the University of Connecticut*

In October 2018, we entered into an exclusive, worldwide option and license agreement (the "UConn Agreement") with the University of Connecticut ("UConn") for the development and commercialization rights to UC1MT, a therapeutic antibody targeting extracellular metallothionein. Under this agreement, we have the option to acquire an exclusive, worldwide license to UC1MT and its underlying patents to develop and commercialize throughout the world in all human indications. If we choose to exercise the option, we would be obligated to pay UConn milestone payments upon the achievement of specified regulatory and commercial milestones, and royalties of a low single-digit percentage of net sales of licensed products.

**Government Regulation**

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act ("FDCA") and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including imposition of a clinical hold, refusal by the FDA to approve applications, withdrawal of an approval, import/export delays, issuance of warning letters and other types of enforcement letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or other governmental entities.

The clinical testing, manufacturing, labeling, storage, distribution, record keeping, advertising, promotion, import, export and marketing, among other things, of our product candidates are governed by extensive regulation by governmental authorities in the United States and other countries. The FDA, under the FDCA, regulates pharmaceutical products in the United States. The steps required before a drug may be approved for marketing in the United States generally include:

- preclinical laboratory tests and animal tests conducted under GLP;
- the submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical trials commence;
- approval by an independent institutional review board ("IRB"), representing each clinical site before each clinical trial may be initiated;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the product for each indication and conducted in accordance with Good Clinical Practices ("GCP");
- the preparation and submission to the FDA of an NDA;
- FDA acceptance, review and approval of the NDA, which might include an Advisory Committee review;
- satisfactory completion of an FDA inspection of the manufacturing facilities at which the product, or components thereof, are made to assess compliance with current Good Manufacturing Practices ("cGMPs").

The testing and approval process requires substantial time, effort and financial resources, and the receipt and timing of any approval is uncertain. The FDA may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

*Preclinical and Human Clinical Trials in Support of an NDA*

Preclinical studies include laboratory evaluations of the product candidate, as well as *in vitro* and animal studies to assess the potential safety and efficacy of the product candidate. The conduct of preclinical trials is subject to federal regulations and requirements including GLP regulations. The results of the preclinical studies, together with manufacturing information and

analytical data, among other things, are submitted to the FDA as part of the IND, which must become effective before clinical trials may be commenced. The IND will become effective automatically 30 days after receipt by the FDA, unless the FDA raises concerns or questions about the conduct of the trials as outlined in the IND prior to that time. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can proceed. The FDA may nevertheless initiate a clinical hold after the 30 days if, for example, significant public health risks arise.

Clinical trials involve the administration of the product candidate to human subjects under the supervision of qualified investigators in accordance with GCP requirements. Each clinical trial must be reviewed and approved by an IRB at each of the sites at which the trial will be conducted. The IRB will consider, among other things, ethical factors, the safety of human subjects and the possible liability of the institution.

Clinical trials are typically conducted in three sequential phases prior to approval, but the phases may overlap or be combined. These phases generally include the following:

*Phase 1.* Phase 1 clinical trials represent the initial introduction of a product candidate into human subjects, frequently healthy volunteers. In Phase 1, the product candidate is usually tested for safety, including adverse effects, dosage tolerance, absorption, distribution, metabolism, excretion and pharmacodynamics.

*Phase 2.* Phase 2 clinical trials usually involve studies in a limited patient population to (1) evaluate the efficacy of the product candidate for specific indications, (2) determine dosage tolerance and optimal dosage and (3) identify possible adverse effects and safety risks.

*Phase 3.* If a product candidate is found to be potentially effective and to have an acceptable safety profile in Phase 2 clinical trials, the clinical trial program will be expanded to Phase 3 clinical trials to further demonstrate clinical efficacy, optimal dosage and safety within an expanded patient population at geographically dispersed clinical trial sites.

*Phase 4.* clinical trials may be conducted after approval to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of drugs approved under accelerated approval regulations, or when otherwise requested by the FDA in the form of post-market requirements or commitments. Failure to promptly conduct any required Phase 4 clinical trials could result in enforcement action or withdrawal of approval.

A Phase 2/3 trial design, which we are using in ourBHV-3500 and troriluzole development programs, is often used in the development of pharmaceutical and biological products. The trial includes Phase 2 elements, such as an early interim analysis of safety or activity, and Phase 3 elements, such as larger patient populations with less restrictive enrollment criteria. The early interim analysis of clinical or physiologic activity and/or safety allows the study to be stopped, changed or continued before a large number of patients have been enrolled, while still allowing all data from enrolled patients to count in the analysis used to support approval.

*Submission and Review of an NDA*

The results of preclinical studies and clinical trials, together with detailed information on the product's manufacture, composition, quality, controls and proposed labeling, among other things, are submitted to the FDA in the form of an NDA, requesting approval to market the product. The application must be accompanied by a significant user fee payment, which typically increases annually, although waivers may be granted in limited cases. The FDA has substantial discretion in the approval process and may refuse to accept any application or decide that the data is insufficient for approval and require additional preclinical, clinical or other studies.

Once an NDA has been accepted for filing, which occurs, if at all, 60 days after submission, the FDA sets a user fee goal date that informs the applicant of the specific date by which the FDA intends to complete its review. This is typically 10 months from the date that the FDA accepts the application for filing for standard review NDAs (*i.e.*, NDAs seeking approval of drugs that are not new molecular entities). The review process can be extended by FDA requests for additional information or clarification. The FDA reviews NDAs to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMPs to assure and preserve the product's identity, strength, quality and purity. Before approving an NDA, the FDA typically will inspect the facilities at which the product is manufactured and will not approve the product unless the manufacturing facilities comply with cGMPs. Additionally, the FDA will typically inspect one or more clinical trial sites for compliance with GCP and integrity of the data supporting safety and efficacy.

During the approval process, the FDA also will determine whether a risk evaluation and mitigation strategy ("REMS") is necessary to assure the safe use of the product. If the FDA concludes a REMS is needed, the sponsor of the application must submit a proposed REMS, and the FDA will not approve the application without an approved REMS, if required. A REMS can substantially increase the costs of obtaining approval. The FDA could also require a special warning, known as a boxed warning, to be included in the product label in order to highlight a particular safety risk. The FDA may also convene an

advisory committee of external experts to provide input on certain review issues relating to risk, benefit and interpretation of clinical trial data. The FDA may delay approval of an NDA if applicable regulatory criteria are not satisfied and/or the FDA requires additional testing or information. The FDA may require post-marketing testing and surveillance to monitor safety or efficacy of a product.

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA will issue either an approval of the NDA or a Complete Response Letter, detailing the deficiencies in the submission and the additional testing or information required for reconsideration of the application. Even with submission of this additional information, the FDA may ultimately decide that the application does not satisfy the regulatory criteria for approval.

***Post-Approval Requirements***

Approved drugs that are manufactured or distributed in the United States 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. After approval, most changes to the approved product, such as adding new indications or other labeling claims and some manufacturing and supplier changes are subject to prior FDA review and approval. There also are continuing, annual program user fee requirements for marketed products, as well as new application fees for certain supplemental applications.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance programs to further assess and monitor the product's safety and effectiveness after commercialization. The FDA may also require a REMS, which could involve requirements for, among other things, medication guides, special trainings for prescribers and dispensers, patient registries, and elements to assure safe use.

In addition, entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. The FDA has promulgated specific requirements for drug cGMPs. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may issue enforcement letters or withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Corrective action could delay product distribution and require significant time and financial expenditures. Later discovery of previously unknown problems with a product, including AEs of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies 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, suspension of the approval, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve applications or supplements to approved applications, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including investigation by federal and state authorities.

***Section 505(b)(2) NDAs***

As an alternative path to FDA approval for modifications to formulations or uses of drugs previously approved by the FDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments. A Section 505(b)(2) NDA is an application that contains full reports of investigations of safety and effectiveness, but where at least some of the information required for approval comes from studies not conducted by, or for, the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. This type of application permits reliance for such approvals on literature or on an FDA finding of safety, effectiveness or both for an approved drug product. As such, under Section 505(b)(2), the FDA may rely, for approval of an NDA, on data not developed by the applicant. The FDA may also require companies to perform additional studies or measurements, including clinical trials, to support the change from the approved branded reference drug. The FDA may then approve the new product candidate for the new indication sought by the 505(b)(2) applicant.

Our clinical programs for troriluzole for the treatment of SCA and BHV-0223 for the treatment of ALS are each based on a regulatory pathway under section 505(b)(2) of the FDCA that allows reference to data on riluzole for the purpose of safety assessments.

***Orange Book Listing***

In seeking approval for a drug through an NDA, including a 505(b)(2) NDA, applicants are required to list with the FDA certain patents whose claims cover the applicant's product or an approved method of using the product. Upon approval of an NDA, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, known as the Orange Book. Any applicant who files an Abbreviated New Drug Application ("ANDA"), seeking approval of a generic equivalent version of a drug listed in the Orange Book or a 505(b)(2) NDA referencing a drug listed in the Orange Book must certify, for each patent listed in the Orange Book for the referenced drug, to the FDA that (1) no patent information on the drug product that is the subject of the application has been submitted to the FDA, (2) such patent has expired, (3) if such patent has not expired, the date on which it expires or (4) such patent is invalid, unenforceable, or will not be infringed upon by the manufacture, use or sale of the drug product for which the application is submitted. The fourth certification described above is known as a paragraph IV certification. A notice of the paragraph IV certification must be provided to each owner of the patent that is the subject of the certification and to the holder of the approved NDA to which the ANDA or 505(b)(2) application refers. The applicant may also elect to submit a "section viii" statement certifying that its proposed label does not contain (or carves out) any language regarding the patented method-of- use rather than certify to a listed method-of-use patent. This section viii statement does not require notice to the patent holder or NDA owner. There might also be no relevant patent certification.

If the reference NDA holder and patent owners assert a patent challenge directed to one of the Orange Book listed patents within 45 days of the receipt of the paragraph IV certification notice, the FDA is prohibited from approving the application until the earlier of 30 months from the receipt of the paragraph IV certification, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the applicant. Even if the 45 days expire, a patent infringement lawsuit can be brought and could delay market entry, but it would not extend the FDA-related 30-month stay of approval.

The ANDA or 505(b)(2) application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the branded reference drug has expired as described in further detail below.

***Non-Patent Exclusivity***

In addition to patent exclusivity, the holder of the NDA for the listed drug may be entitled to a period of non-patent exclusivity, during which the FDA cannot approve an ANDA or 505(b)(2) application that relies on the listed drug.

A drug, including one approved under a 505(b)(2) application, may obtain a three-year period of non-patent market exclusivity for a particular condition of approval, or change to a marketed product, such as a new formulation for a previously approved product, if one or more new clinical studies (other than bioavailability or bioequivalence studies) was essential to the approval of the application and was conducted/sponsored by the applicant. Should this occur, the FDA would be precluded from approving any ANDA or 505(b)(2) application for the protected modification until after that three-year exclusivity period has run. However, the FDA can accept an application and begin the review process during the three-year exclusivity period. A 505(b)(2) NDA may also be subject to a five-year exclusivity period for a new chemical entity, whereby the FDA will not accept for filing, with limited exception, a product seeking to rely upon the FDA's findings of safety or effectiveness for such new chemical entity.

***Orphan Drugs***

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition affecting fewer than 200,000 individuals in the United States, or in other limited cases. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process, though companies developing orphan drugs may be eligible for certain incentives, including tax credits for qualified clinical testing. In addition, an NDA for a product that has received orphan drug designation is not subject to a prescription drug user fee unless the application includes an indication other than the rare disease or condition for which the drug was designated. A Company must request orphan drug designation before submitting an NDA.

Generally, if a product that has orphan drug designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same active moiety for the same indication for seven years, except in limited circumstances, such as another drug's showing of clinical superiority over the drug with orphan exclusivity. Competitors, however, may receive approval of different active moieties for the same indication or obtain approval for the same active moiety for a different indication. In some cases, orphan drug status is contingent on a product with an orphan drug designation showing that it is clinically superior to a previously approved product or products.

***Foreign Regulation***

In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable foreign regulatory authorities before we can commence clinical trials or marketing of the product in foreign countries and jurisdictions. Although many of the issues discussed above with respect to the United States apply similarly in the context of the European Union and other geographies, the approval process varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

***Coverage, Reimbursement and Pricing***

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval. In the United States and foreign markets, sales of any products for which we receive regulatory approval for commercial sale will depend, in part, on the availability of coverage and the adequacy of reimbursement from third-party payors. Third-party payors include government authorities, and private entities, such as managed care organizations, private health insurers and other organizations. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication. Moreover, a third-party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. For example, the payor's reimbursement payment rate may not be adequate or may require co-payments that patients find unacceptably high. Additionally, coverage and reimbursement for products can differ significantly from payor to payor. The Medicare and Medicaid programs increasingly are used as models for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. However, one third-party payor's decision to cover a particular product does not ensure that other payors will also provide coverage for the product, or will provide coverage at an adequate reimbursement rate. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Further, some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they provide reimbursement for use of such therapies.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of products and services, in addition to their safety and efficacy. To obtain coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies to demonstrate the medical necessity and cost-effectiveness of our product. These studies will be in addition to the studies required to obtain regulatory approvals. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. Thus, obtaining and maintaining reimbursement status is time-consuming and costly.

The U.S. and foreign governments regularly consider reform measures that affect health care coverage and costs. For example, the U.S. and state legislatures have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription products. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act ("collectively, the ACA") contains provisions that may 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. The Centers for Medicare and Medicaid Services ("CMS") may develop new payment and delivery models, such as bundled payment models. For example, the U.S. Department of Health and Human Services ("HHS") moved 30% of Medicare payments to alternative payment models tied to the quality or value of services by 2016. Additionally, HHS had set a goal of moving 50% of Medicare payments into these alternative payment models by the end of 2018, but due to a policy shift under the Trump Administration, it is unclear how and when such changes will be implemented. Adoption of government controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for our products.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, the focus on cost containment measures, particularly in the United States, has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if we attain favorable coverage and reimbursement status for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

***European Union Coverage Reimbursement and Pricing***

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies, or so called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or may instead adopt a system of direct or indirect controls on the profitability of the company.

***Healthcare Laws and Regulations***

Physicians, other healthcare providers, and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers and third-party payors are and will be subject to various federal, state and foreign fraud and abuse laws and other healthcare laws and regulations. These laws and regulations may impact, among other things, our arrangements with third-party payors, healthcare professionals who participate in our clinical research programs, healthcare professionals and others who purchase, recommend or prescribe our approved products, and our proposed sales, marketing, distribution, and education programs. The U.S. federal and state healthcare laws and regulations that may affect our ability to operate include, without limitation, the following:

- The federal Anti-Kickback Statute, which prohibits persons from, among other things, knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federally funded healthcare programs, such as Medicare and Medicaid. The term "remuneration" has been broadly interpreted to include anything of value;

- The federal civil and criminal false claims laws, including, without limitation, the federal civil monetary penalties law and the civil False Claims Act (which can be enforced by private citizens through *qui tam* actions), prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment of federal funds, and knowingly making, or causing to be made, a false record or statement material to a false or fraudulent claim to avoid, decrease or conceal an obligation to pay money to the federal government;

- The federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") which imposes criminal liability for executing or attempting to execute a scheme to defraud any healthcare benefit program and creates federal criminal laws that prohibit knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH") and its implementing regulations, which imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without the appropriate authorization by entities subject to the law, such as healthcare providers, health plans, and healthcare clearinghouses and their respective business associates;

- The federal transparency requirements under the Physician Payments Sunshine Act, created under the ACA, which requires certain manufacturers of drugs, devices, biologics and medical supplies reimbursed under Medicare, Medicaid ("CHIP") to report to HHS information related to payments and other transfers of value provided to physicians and teaching hospitals and physician ownership and investment interests; and

- Analogous state laws and regulations, such as state anti-kickback and false claims laws, that impose similar restrictions and may apply to items or services reimbursed by non-governmental third-party payors, including private insurers; state laws that require pharmaceutical companies to implement compliance programs, comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or to track and report gifts, compensation and other remuneration provided to physicians and other health care providers; and state health information privacy and data breach notification laws, which govern the collection, use, disclosure, and protection of health-related and other personal information, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

We will be required to spend substantial time and money to ensure that our business arrangements with third parties comply with applicable healthcare laws and regulations. Recent healthcare reform legislation has strengthened these federal and state healthcare laws. For example, the ACA amends the intent requirement of the federal Anti-Kickback Statute and criminal healthcare fraud statutes to clarify that liability under these statutes does not require a person or entity to have actual knowledge of the statutes or a specific intent to violate them. Moreover, the ACA provides that the government may assert that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act. Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws.

Violations of these laws can subject us to criminal, civil and administrative sanctions including monetary penalties, damages, fines, disgorgement, individual imprisonment, and exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, 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 reputational harm, we may be required to curtail or restructure our operations. Moreover, we expect that there will continue to be federal and state laws and regulations, proposed and implemented, that could impact our future operations and business.

***Healthcare Reform***

The legislative landscape in the United States continues to evolve. There have been a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the United States federal and state levels that seek to reduce healthcare costs. In March 2010, the ACA was enacted, which includes measures that have significantly changed health care financing by both governmental and private insurers. The provisions of the ACA of importance to the pharmaceutical and biotechnology industry are, among others, the following:

- an annual, non-deductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, which is apportioned among these entities according to their market share in certain government healthcare programs;

- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (and 70% commencing January 1, 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer’s outpatient drugs to be covered under Medicare Part D;

- new requirements to report certain financial arrangements with physicians and certain others, including reporting “transfers of value” made or distributed to prescribers and other healthcare providers and reporting investment interests;

- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- extension of a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of the Center for Medicare Innovation at the Centers for Medicare and Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

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. President Trump has signed two Executive Orders designed to delay the implementation of any 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 23, 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 on non-exempt medical devices.

In addition, other federal health reform measures have been proposed and adopted in the United States since the ACA was enacted. For example, as a result of the Budget Control Act of 2011, providers are subject to Medicare payment reductions of 2% per fiscal year through 2025 unless additional Congressional action is taken. Further, the American Taxpayer Relief Act of 2012 reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments from providers from three to five years. The Medicare Access and CHIP Reauthorization Act of 2015 also introduced a quality payment program under which certain individual Medicare providers will be subject to certain incentives or penalties based on new program quality standards. Payment adjustments for the Medicare quality payment program will begin in 2019. At this time, it is unclear how the introduction of the quality payment program will impact overall physician reimbursement under the Medicare program.

Further, there have been several recent Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the costs of prescription pharmaceuticals in the United States has also been the subject of considerable discussion, and members of Congress and the Trump Administration have stated that they will address such costs through new legislative and administrative measures. At the state level, legislatures are increasingly aggressive in 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. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

***The Foreign Corrupt Practices Act***

The Foreign Corrupt Practices Act (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.

**Employees**

As of December 31, 2018, we employed 63 employees. All of our employees are located in the United States. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

**Information about Segments**

We currently operate in a single business segment developing a portfolio of innovative, late-stage product candidates targeting neurological diseases, including rare disorders. See additional information in our financial statements contained in Part II, Item 8 of this Annual Report.

**Corporate Information**

We were incorporated as a business company limited by shares organized under the laws of the British Virgin Islands in September 2013. Our registered office is located at P.O. Box 173, Road Town, Tortola, British Virgin Islands and our telephone number is +1 (284) 852-3000. Our U.S. office and the office of our U.S. subsidiary is located at 215 Church Street, New Haven, Connecticut 06510 and our telephone number is (203) 404-0410.

**Available Information**

Our internet website address is www.biohavenpharma.com. In addition to the information about us and our subsidiaries contained in this Annual Report, information about us can be found on our website. Our website and information included in or linked to our website are not part of this Annual Report.

Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, are available free of charge through our website as soon as reasonably practicable after they are electronically filed with or furnished to the Securities and Exchange Commission ("SEC"). The public may read and copy the 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. Additionally, the SEC maintains an internet site that contains reports, proxy and information statements and other information. The address of the SEC's website is www.sec.gov.

## Item 1A. Risk Factors

*You should carefully consider the risks described below, as well as general economic and business risks and the other information in this Annual Report on Form 10-K. The occurrence of any of the events or circumstances described below or other adverse events could have a material adverse effect on our business, results of operations and financial condition and could cause the trading price of our common shares to decline. Additional risks or uncertainties not presently known to us or that we currently deem immaterial may also harm our business.*

### Risks Related to Our Financial Position and Need for Additional Capital

***We have a limited operating history and have never generated any product revenues, which may make it difficult to evaluate the success of our business to date and to assess our future viability.***

We were incorporated in 2013, and our operations to date have been largely focused on organizing and staffing our company, raising capital and in-licensing the rights to, and advancing the development of, our product candidates, including conducting preclinical studies and clinical trials. We have not yet demonstrated an ability to obtain marketing approvals for any product candidates, manufacture products on a commercial scale, or arrange for a third party to do so on our behalf, or conduct

sales and marketing activities necessary for successful commercialization. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing products.

We expect our financial condition and operating results to continue to fluctuate from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. We will need to eventually transition from a company with a research and development focus to a company capable of undertaking commercial activities. We may encounter unforeseen expenses, difficulties, complications and delays, and may not be successful in such a transition.

***We have incurred significant operating losses since inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future and may never achieve or maintain profitability.***

Since our inception, we have incurred significant operating losses. Our net loss was $240.9 million and $127.2 million for the year ended December 31, 2018 and for the year ended December 31, 2017, respectively. As of December 31, 2018, we had an accumulated deficit of $443.6 million. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. None of our product candidates have been approved for marketing in the United States, or in any other jurisdiction, and may never receive such approval. It could be several years, if ever, before we have a commercialized product that generates significant revenues. As a result, we are uncertain when or if we will achieve profitability and, if so, whether we will be able to sustain it. The net losses we incur may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially as we:

- complete our long-term safety study of rimegepant, Phase 1 supporting trials of rimegepant and our ongoing Phase 3 clinical trial to evaluate rimegepant as a preventive therapy for migraine;
- complete the ongoing extension phase of the Phase 2/3 clinical trial of troriluzole in SCA and our ongoing Phase 2/3 trials of troriluzole in OCD, Alzheimer's disease and GAD and, conduct a second randomized controlled trial to assess the efficacy of troriluzole in SCA;
- conduct support activities for future clinical trials of BHV-5000;
- conduct our planned Phase 2/3 clinical trial of BHV-3500 and related support activities;
- conduct out planned Phase 3 clinical trial of verdiperstat in multiple system atrophy;
- continue to initiate and progress other supporting studies required for regulatory approval of our product candidates, including long-term safety studies, drug-drug interaction studies, preclinical toxicology and carcinogenicity studies;
- make required milestone and royalty payments under the license agreements by which we acquired some of the rights to our product candidates;
- make required royalty payments to RPI Finance Trust ("RPI"), under the funding agreement, entered into June 2018, between us and RPI ("Funding Agreement");
- initiate preclinical studies and clinical trials for any additional indications for our current product candidates and any future product candidates that we may pursue;
- continue to build our portfolio of product candidates through the acquisition or in-license of additional product candidates or technologies;
- continue to develop, maintain, expand and protect our intellectual property portfolio;
- pursue regulatory approvals for our current and future product candidates that successfully complete clinical trials, including rimegepant and BHV-0223;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any product candidate for which we may obtain marketing approval;
- hire additional clinical, medical, commercial, and development personnel; and
- incur additional legal, accounting and other expenses in operating as a public company.

In addition to the fluctuation of our operating expenses, our financial results may also be materially impacted in the future by material changes in the operating results of Kleo Pharmaceuticals, Inc. ("Kleo") or if we conclude that the value of our investment in Kleo is impaired and, as a result, we are required by U.S. GAAP to write down the carrying value of our investment.

To become and remain profitable, we must develop and eventually commercialize one or more product candidates with significant market potential. This will require us to be successful in a range of challenging activities, including completing

clinical trials of our product candidates, developing commercial scale manufacturing processes, obtaining marketing approval, manufacturing, marketing and selling any current and future product candidates for which we may obtain marketing approval, and satisfying any post-marketing requirements. We are only in the preliminary stages of most of these activities and, in some cases, have not yet commenced certain of these activities.

We may never succeed in any or all of these activities and, even if we do, we may never generate sufficient revenue to achieve profitability. In addition, our potential obligation to pay RPI royalties on future sales of rimegepant, BHV-3500 and certain derivative compounds thereof pursuant to the Funding Agreement would impact the profitability of these products.

Because of the numerous risks and uncertainties associated with product development, we are unable to accurately predict the timing or amount of expenses or when, or if, we will obtain marketing approval to commercialize any of our product candidates. If we are required by the FDA or other regulatory authorities such as the EMA or the National Medical Products Administration to perform studies and trials in addition to those currently expected, or if there are any delays in the development, or in the completion of any planned or future preclinical studies or clinical trials of our current or future product candidates, our expenses could increase and profitability could be further delayed.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company also could cause you to lose all or part of your investment.

***We will need substantial additional funding to pursue our business objectives. If we are unable to raise capital when needed or on terms favorable to us, we could be forced to curtail our planned operations and the pursuit of our growth strategy.***

Identifying potential product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. We expect our expenses to increase in connection with our ongoing activities, particularly as we continue to develop our product candidates. Our expenses could increase beyond our current expectations if the FDA requires us to perform clinical trials and other studies in addition to those that we currently anticipate. For example, for our troriluzole clinical program, we are planning to conduct an additional Phase 3 clinical trial in SCA incorporating feedback from the FDA in response to discussion that we had with the FDA regarding proposed modifications to the SARA scale, the primary endpoint in the trial. With regard to our BHV-5000 program, due to the small number of patients with CRPS and Rett syndrome, we believe that BHV-5000 will require only a single pivotal trial for each disorder. However, the FDA ordinarily requires two well-controlled clinical trials prior to marketing approval of a product candidate. If the FDA requires us to conduct additional clinical trials of troriluzole or BHV-5000, or any of our other product candidates, we would incur substantial additional, unanticipated expenses in order to obtain regulatory approval of those product candidates.

In addition, our product candidates, if approved, may not achieve commercial success. Our revenue, if any, will be derived from sales of products that we do not expect to be commercially available for a number of years, if at all. Additionally, if we obtain marketing approval for our product candidates, we expect to incur significant expenses related to manufacturing, marketing, sales and distribution and, with respect to certain of our product candidates, the payment of milestone and royalty fees. In addition, in June 2018 we entered into the Funding Agreement with RPI pursuant to which we issued to RPI the right to receive certain revenue participation payments, subject to certain reductions, based on the future global net sales of pharmaceutical products containing the compounds rimegepant or BHV-3500 and certain derivative compounds thereof, in exchange for $100 million. Even if we are able to obtain marketing approval for rimegepant or BHV-3500, we cannot guarantee that sales of such products, if any, will be sufficiently profitable due to our obligations under the Funding Agreement. Furthermore, we expect to incur additional costs associated with operating as a public company.

As of December 31, 2018, we had cash of $264.2 million. We expect that our existing cash will be sufficient to fund our planned operating expenses, financial commitments and other cash requirements for at least twelve months from the date of filing of this report. This estimate is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we expect. Changes may occur beyond our control that would cause us to consume our available capital before that time, including changes in and progress of our development activities and changes in regulation. Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of our ongoing and planned preclinical studies and clinical trials for our product candidates;
- the timing and amount of milestone and royalty payments we are required to make under our license agreements and the Funding Agreement;
- the extent to which we in-license or acquire other product candidates and technologies;

- the number and development requirements of other product candidates that we may pursue, and other indications for our current product candidates that we may pursue;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs and timing of future commercialization activities, including drug manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- our ability to establish strategic collaborations for the development or commercialization of some of our product candidates; and
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims brought by third parties against us.

We will require additional capital to complete our planned clinical development programs for our current product candidates to seek regulatory approval. If we receive regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution. Any additional capital raising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our current and future product candidates, if approved.

In addition, we cannot guarantee that future financing will be available on a timely basis, in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our shareholders and the issuance of additional securities by us, whether equity or debt, or the market perception that such issuances are likely to occur, could cause the market price of our common shares to decline. As a result, we may not be able to access the capital markets as frequently as comparable U.S. companies. If we are unable to obtain funding on a timely basis on acceptable terms, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product candidates, if approved, or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired.

***We are subject to significant obligations, including to potentially make significant payments under the license agreements by which we acquired the rights to several of our product candidates and under our funding agreement related to rimegepant and BHV-3500.***

In July 2016, we acquired the rights to rimegepant and another product candidate, BHV-3500, pursuant to a license agreement with BMS, and in October 2016, we acquired the rights to BHV-5000 pursuant to a license agreement with AstraZeneca. We are subject to significant obligations under these agreements, including payment obligations upon achievement of specified milestones and royalties on product sales, as well as other material obligations. We may be obligated to pay BMS up to $127.5 million in development milestones for rimegepant or a derivative thereof, up to $74.5 million in development milestones for any licensed product other than rimegepant, and up to $150.0 million in commercial milestones for each licensed product. In July 2017, we paid BMS $5.0 million due to the achievement of a specified milestone. We may also be obligated to pay AstraZeneca up to $30.0 million in development milestones for licensed products for the treatment of Rett syndrome, up to $60.0 million in development milestones for licensed products for CRPS and indications other than Rett syndrome, and up to $120.0 million in commercial milestones. We are also obligated to pay fixed royalties based on net sales of rimegepant, BHV-3500 and BHV-5000, or any other product that is a licensed product under those agreements. If these payments become due under the terms of our license agreements with BMS and AstraZeneca, we may not have sufficient funds available to meet our obligations and our development efforts may be materially harmed.

In September 2018, we entered into the 2018 AstraZeneca Agreement. Under the 2018 AstraZeneca Agreement, we are obligated to pay milestone payments to AstraZeneca totaling up to $55.0 million upon the achievement of specified regulatory and commercial milestones and up to $50.0 million upon the achievement of specified sales-based milestones. In addition, we will pay AstraZeneca tiered royalties ranging from high single-digit to low double-digits based on net sales of any approved products based on verdiperstat, subject to specified reductions. We may sublicense our rights under the agreement and, if we do so, we will be obligated to pay a portion of any milestone payments received from the sublicensee to AstraZeneca in addition to any milestone payments we would otherwise be obligated to pay.

In addition, our license agreements with BMS and AstraZeneca obligate us to use commercially reasonable efforts to develop and commercialize product candidates, to provide BMS and AstraZeneca with development reports documenting our progress, and to provide them with data from certain clinical trials. In addition, the 2016 AstraZeneca Agreement provides with rights of first negotiation, triggered by their receipt of a summary of certain topline data from certain of our clinical trials, to regain the respective rights we have in-licensed from them. If AstraZeneca exercises their right of first negotiation, we will be

required to negotiate in good faith, as the case may be, for a specified period of time before we can enter into negotiations with third parties to sublicense these rights. AstraZeneca's rights of first negotiation may adversely impact or delay our ability to enter into collaborations with third parties for the development of these compounds. Our license agreement with BMS further provides that any sublicense, other than to an affiliate or a third-party manufacturer, requires BMS' prior written consent, not to be unreasonably withheld or delayed. Each of our license agreements with AstraZeneca further provide that, except with respect to wholly owned subsidiaries, we cannot assign the agreement without their consent, even in the event of a change of control. This could adversely impact or delay our ability to effect certain transactions.

In June 2018, we entered into the Funding Agreement with RPI, which requires us to make revenue participation payments, subject to certain reductions, based on the future global net sales of pharmaceutical products containing the compounds rimegepant or BHV-3500 and certain derivative compounds thereof. The participation rate commences at 2.1 percent on global annual net sales of products up to and equal to $1.5 billion, declining to 1.5 percent on global annual net sales of products exceeding $1.5 billion. If these payments become due under the terms of the Funding Agreement, they will have a negative impact on our cash flows and on the future profitability of rimegepant and BHV-3500.

In addition, under the Funding Agreement, we are obligated to take certain steps to complete clinical trials and commercialize products containing the compounds rimegepant or BHV-3500 and certain derivative compounds thereof. These obligations could adversely impact or delay our ability to develop our other product candidates.

***Raising additional capital may cause dilution to our shareholders, restrict our operations or require us to relinquish rights to our intellectual property or future revenue streams.***

Until such time as we can generate substantial product revenue, if ever, we expect to finance our operations through a combination of equity offerings, debt financings and license and development agreements in connection with any future collaborations. We do not have any committed external source of funds. In the event we seek additional funds, we may raise additional capital through the sale of equity or convertible debt securities. In such an event, our existing shareholders may experience substantial dilution, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of the holders of our common shares. Debt financing, if available, could result in increased fixed payment obligations and may involve agreements that include restrictive covenants, such as limitations on our ability to incur additional debt, make capital expenditures, acquire, sell or license intellectual property rights or declare dividends, and other operating restrictions that could hurt our ability to conduct our business.

Further, if we raise additional capital through collaborations, strategic alliances, or marketing, distribution, licensing or funding arrangements with third parties, we may have to relinquish valuable rights to our intellectual property future revenue streams, research programs or product candidates, or grant licenses on terms that may not be favorable to us.

**Risks Related to the Development of Our Product Candidates**

***We depend entirely on the success of a limited number of product candidates, which are in clinical development. If we do not obtain regulatory approval for and successfully commercialize one or more of our product candidates or we experience significant delays in doing so, we may never become profitable.***

We do not have any products that have received regulatory approval and may never be able to develop marketable product candidates. We expect that a substantial portion of our efforts and expenses over the next few years will be devoted to the development of our product candidates; specifically, the completion of the ongoing extension phase of the Phase 2/3 clinical trial and the conduct and completion of our second randomized controlled trial of troriluzole in SCA, completion of our Phase 2/3 clinical trials of troriluzole in OCD, GAD and Alzheimer's disease and patient tolerability studies, completion of our long-term safety study for rimegepant, completion of a fourth Phase 3 clinical trial of rimegepant for the preventive treatment of migraine; and completion of our Phase 2/3 trials for BHV-3500. As a result, our business currently depends heavily on the successful development, regulatory approval and, if approved, commercialization of these product candidates. We cannot be certain that we will be able to submit an NDA for any of our product candidates within the timeframes we expect, that any NDA we submit will be accepted by the FDA for filing in a timely manner or at all, or that any of our product candidates will receive regulatory approval or will be successfully commercialized even if they receive regulatory approval. The research, testing, manufacturing, safety, efficacy, labeling, approval, sale, marketing and distribution of our product candidates are, and will remain, subject to comprehensive regulation by the FDA and similar foreign regulatory authorities. Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate through pre-clinical studies and clinical trials that the product candidate is safe and effective for use in each target indication. Drug development is a long, expensive and uncertain process, and delay or failure can occur at any stage of any of our clinical trials. Failure to obtain regulatory approval for our product candidates in the United States will prevent us from commercializing and marketing our product candidates. The success of our product candidates will depend on several additional factors, including:

- completing clinical trials that demonstrate their efficacy and safety;

- receiving marketing approvals from applicable regulatory authorities;
- completing any post-marketing studies required by applicable regulatory authorities;
- establishing commercial manufacturing capabilities;
- launching commercial sales, marketing and distribution operations;
- the prevalence and severity of adverse events experienced with our product candidates;
- acceptance of our product candidates by patients, the medical community and third-party payors;
- a continued acceptable safety profile following approval;
- obtaining and maintaining healthcare coverage and adequate reimbursement for our product candidates;
- competing effectively with other therapies, including with respect to the sales and marketing of our product candidates, if approved; and
- qualifying for, maintaining, enforcing and defending our intellectual property rights and claims.

Many of these factors are beyond our control, including the time needed to adequately complete clinical testing, the regulatory submission process, potential threats to our intellectual property rights and changes in the competitive landscape. It is possible that none of our product candidates will ever obtain regulatory approval, even if we expend substantial time and resources seeking such approval. If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully complete clinical trials, obtain regulatory approval or, if approved, commercialize our product candidates, which would materially harm our business, financial condition and results of operations.

***Clinical trials are very expensive, time-consuming and difficult to design and implement and involve uncertain outcomes. Furthermore, results of earlier preclinical studies and clinical trials may not be predictive of results of future preclinical studies or clinical trials.***

The risk of failure for our product candidates is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval. To obtain the requisite regulatory approvals to market and sell any of our product candidates, we must demonstrate through extensive preclinical studies and clinical trials that our product candidates are safe and effective in humans for use in each target indication. Clinical testing is expensive and can take many years to complete, and the outcome is inherently uncertain. Failure can occur at any time during the clinical trial process.

In addition, the results of preclinical studies and earlier clinical trials may not be predictive of the results of later-stage preclinical studies or clinical trials. The results generated to date in preclinical studies or clinical trials for our product candidates do not ensure that later preclinical studies or clinical trials will demonstrate similar results. Further, we have limited clinical data for many of our product candidates. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical and earlier stage clinical trials. In later-stage clinical trials, we will likely be subject to more rigorous statistical analyses than in completed earlier stage clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in later-stage clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials, and we cannot be certain that we will not face similar setbacks. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

For example, the Phase 2 clinical trial of verdiperstat in patients with MSA completed by AstraZeneca failed to meet its primary endpoint of change from baseline in microglia activation assessed by PET. While we believe that directionally positive signals on certain components of the exploratory efficacy endpoint of Unified Multiple System Atrophy Rating Scale ("UMSARS") warrant further study of verdiperstat in MSA, there is no guarantee that future studies of verdiperstat will be successful.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in clinical trial procedures set forth in protocols, differences in the size and type of the patient populations, adherence to the dosing regimen, and the rate of dropout among clinical trial participants. For example, to date less than 65 subjects with ALS have been dosed with BHV-0223 and although adverse events generally have been mild to moderate in severity it is possible that additional novel adverse events may emerge or severity profile may change. In addition, we plan to initiate a second randomized, controlled clinical trial of troriluzole in SCA in the second quarter of 2019 which will incorporate trial design modifications compared to our Phase 2/3 clinical trial, including the use of a modified SARA scale to measure patient improvement. We cannot predict the impact these modifications may have on the results of this second trial.

Additionally, the data we have presented herein and upon which we have based our determination to proceed with the clinical development of troriluzole in SCA is drawn from post-hoc analyses of data subsets from our Phase 2/3 clinical trial, as well as comparisons to a natural history study cohort. While we believe these data may be useful in informing the design of our future randomized, controlled clinical trial of troriluzole, post-hoc analyses performed after unmasking trial results can result in the introduction of bias and may not be predictive of success in future clinical trials.

If we fail to produce positive results in our planned pre-clinical studies or clinical trials of any of our product candidates, the development timeline and regulatory approval and commercialization prospects for our product candidates, and, correspondingly, our business and financial prospects, would be materially adversely affected.

***We have limited experience in drug discovery and drug development, and we have never had a drug approved.***

Because we in-licensed rimegepant and BHV-3500 from BMS and BHV-5000 and verdiperstat from AstraZeneca, we were not involved in and had no control over the preclinical and clinical development of these product candidates prior to entering into these in-license agreements. In addition, we are relying on BMS and AstraZeneca to have conducted such research and development in accordance with the applicable protocol, legal, regulatory and scientific standards, having accurately reported the results of all clinical trials conducted prior to our acquisition of the applicable product candidate, and having correctly collected and interpreted the data from these studies and trials. To the extent any of these has not occurred, our expected development time and costs may be increased, which could adversely affect our prospects for marketing approval of, and receiving any future revenue from, these product candidates. We have only recently submitted our first NDA, for BHV-0223, and have never had a drug approved.

***Clinical trials may be delayed, suspended or terminated for many reasons, which will increase our expenses and delay the time it takes to develop our product candidates.***

We may experience delays in our ongoing or future preclinical studies or clinical trials, and we do not know whether future preclinical studies or clinical trials will begin on time, need to be redesigned, enroll an adequate number of patients on time or be completed on schedule, if at all. The commencement and completion of clinical trials for our clinical product candidates may be delayed, suspended or terminated as a result of many factors, including:

- the FDA disagreeing as to the design, protocol or implementation of our clinical trials;
- the FDA's decision not to allow us to proceed to initiate clinical trials upon our submission of an IND or a request to reactivate an IND;
- the delay or refusal of regulators or institutional review boards ("IRBs") to authorize us to commence a clinical trial at a prospective trial site;
- changes in regulatory requirements, policies and guidelines;
- delays or failure to reach agreement on acceptable terms with prospective clinical research organization ("CROs") and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites; delays in patient enrollment and variability in the number and types of patients available for clinical trials;
- the inability to enroll a sufficient number of patients in trials, particularly in orphan indications, to observe statistically significant treatment effects in the trial;
- having clinical sites deviate from the trial protocol or dropping out of a trial;
- negative or inconclusive results from ongoing preclinical studies or clinical trials, which may require us to conduct additional preclinical studies or clinical trials or to abandon projects that we expect to be promising;
- safety or tolerability concerns that could cause us to suspend or terminate a trial if we find that the participants are being exposed to unacceptable health risks;
- reports from pre-clinical or clinical testing of other similar therapies that raise safety or efficacy concerns;
- regulators or IRBs requiring that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or safety concerns, among others;
- lower than anticipated retention rates of patients and volunteers in clinical trials;
- our CROs or clinical trial sites failing to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, deviating from the protocol or dropping out of a trial;
- delays relating to adding new clinical trial sites;

- difficulty in maintaining contact with patients after treatment, resulting in incomplete data;
- delays in establishing the appropriate dosage levels;
- the quality or stability of the product candidate falling below acceptable standards;
- the inability to produce or obtain sufficient quantities of the product candidate to commence or complete clinical trials; and
- exceeding budgeted costs due to difficulty in accurately predicting costs associated with clinical trials.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs or Ethics Committees of the institutions at which such trials are being conducted, by the Data Safety Monitoring Board for such trial or by the FDA or other regulatory authorities. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements, including the FDA's current Good Clinical Practice ("GCP") regulations, or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

In order to commence our additional planned clinical trials of BHV-5000 and BHV-5000 , the FDA has required that we conduct additional nonclinical toxicology studies. There is no assurance that these studies will be successful or that we will be permitted to conduct further clinical studies of BHV-5000.

If we experience delays in the commencement or completion of any clinical trial of our product candidates, or if any of our clinical trials are terminated, the commercial prospects of our product candidates may be harmed, and our ability to generate product revenue from sales of any of these product candidates will be delayed or not realized at all.

We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenue from product sales. Any of these occurrences may significantly harm our business, financial condition and prospects. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Significant preclinical study or 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 and impair our ability to successfully commercialize our product candidates.

Additionally, we regularly assess our portfolio based on emerging data from pre-clinical studies and clinical trials, and we may make changes to expand or discontinue programs based on these assessments. Expansion of the number or scope of clinical trials may result in additional expenses compared to our expectations.

***The regulatory approval process of the FDA and comparable foreign jurisdictions is lengthy, time-consuming and unpredictable.***

Our future success is dependent upon our ability to successfully develop, obtain regulatory approval for and then successfully commercialize one or more of our product candidates. The time required to obtain approval by the FDA is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval is generally uncertain, may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval. Neither we nor any future collaborator is permitted to market any of our product candidates in the United States or abroad until we receive regulatory approval of an NDA from the FDA or approval from the EMA, National Medical Products Administration or other applicable foreign regulatory agency.

Prior to obtaining approval to commercialize a product candidate in any jurisdiction, we must demonstrate to the satisfaction of the FDA, EMA, National Medical Products Administration or any comparable foreign regulatory agency, that such product candidates are safe and effective for their intended uses. Results from preclinical studies and clinical trials can be interpreted in different ways. The FDA, EMA, National Medical Products Administration or any comparable foreign regulatory agency can delay, limit or deny approval of our product candidates or require us to conduct additional preclinical or clinical testing or abandon a program for many reasons, including:

- the FDA, EMA, National Medical Products Administration or the applicable foreign regulatory agency's disagreement with the number, design, conduct or implementation of our preclinical studies and clinical trials;

- negative or ambiguous results from our clinical trials or results that may not meet the level of statistical significance required by the FDA, EMA, National Medical Products Administration or any comparable foreign regulatory agency for approval;
- serious and unexpected drug-related side effects experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- our inability to demonstrate to the satisfaction of the FDA, EMA, National Medical Products Administration or the applicable foreign regulatory agency that our product candidates are safe and effective for their proposed indications;
- the FDA's, EMA's, National Medical Products Administration's or the applicable foreign regulatory agency's disagreement with the interpretation of data from preclinical studies or clinical trials;
- actions by the CROs that we retain to conduct our preclinical studies and clinical trials, which are outside of our control and that materially adversely impact our preclinical studies and clinical trials;
- the FDA's, EMA's, National Medical Products Administration's or other applicable foreign regulatory agencies' disagreement with the interpretation of data from preclinical studies or clinical trials;
- our inability to demonstrate the clinical and other benefits of our product candidates outweigh any safety or other perceived risks;
- the FDA's, EMA's, National Medical Products Administration's or the applicable foreign regulatory agency's requirement for additional preclinical studies or clinical trials;
- the FDA's, EMA's, National Medical Products Administration's or the applicable foreign regulatory agency's disagreement regarding the formulation, labeling or the specifications of our product candidates;
- the FDA's, EMA's, National Medical Products Administration's or the applicable foreign regulatory agency's failure to approve the manufacturing processes or facilities of third-party manufacturers with which we contract; or
- the potential for approval policies or regulations of the FDA, EMA, National Medical Products Administration or the applicable foreign regulatory agencies to significantly change in a manner rendering our clinical data insufficient for approval.

For example, with respect to our second planned randomized, controlled clinical trial of troriluzole for the treatment of SCA, we undertook discussions with the FDA regarding the acceptability of the primary endpoint and necessary secondary endpoints, including our proposal to use a modified SARA scale. In our Phase 2/3 clinical trial, the FDA stated that while certain items measured by the SARA scale appeared capable of reflecting a clinically meaningful benefit for patients depending on how the scoring of those items is defined, the use of the SARA scale was not appropriate as a primary endpoint in the trial. Based on our post-hoc analyses of data from the open-label extension phase of the trial, we proposed modifications to the SARA scale that we believe may address some of these shortcomings. Based on feedback received from the FDA, we are incorporating trial design modifications that include utilization of a modified SARA scale, However, notwithstanding the feedback that we have recieved from the FDA, there remains substantial risk that even if we receive favorable results from this second trial, the FDA or any foreign regulatory agency may nevertheless conclude that results obtained using the modified SARA scale would not be an adequate basis for approval.

BHV-0223 40mg met bioequivalent criteria (AUC and Cmax) with generic riluzole 50mg tablets. Since the currently approved riluzole is associated with a negative food effect (lower AUC and Cmax when administered with high fat meals), a food assessment was performed within the BHV-0223 Phase 1 trial. Topline results from the food effect assessment, demonstrated bioequivalent AUC exposure for BHV-0223 40 mg under both fed and fasting states. However, Cmax concentrations were lowered by more than 20% under the fed state. We believe that BHV-0223's property of maintaining therapeutic AUC exposures regardless of feeding state is clinically important for patients. Ultimately, the FDA will determine the labeling of BHV-0223 with regard to the effect of feeding, which may impact our marketing of BHV-0223 if it is approved.

Any of our current or future product candidates could take a significantly longer time to gain regulatory approval than expected or may never gain regulatory approval. This could delay or eliminate any potential product revenue by delaying or terminating the potential commercialization of our product candidates.

Of the large number of drugs in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, financial condition, results of operations and prospects.

FDA guidance regarding the approval of drugs for the acute treatment of migraine has recently changed. No drug has been approved under the new guidance, and it is not certain how such guidance will be interpreted and applied by the FDA. We intend to seek advice and guidance from the FDA which may include requesting a pre-NDA meeting with the FDA prior to the submission of an NDA for any of our product candidates. If the feedback we receive is different from what we currently anticipate, this could delay the development and regulatory approval process for these product candidates. We generally plan to seek regulatory approval to commercialize our product candidates in the United States, the European Union and other key global markets. To obtain regulatory approval in other countries, we must comply with numerous and varying regulatory requirements of such other countries regarding safety, efficacy, chemistry, manufacturing and controls, clinical trials, commercial sales, pricing and distribution of our product candidates. Even if we are successful in obtaining approval in one jurisdiction, we cannot ensure that we will obtain approval in any other jurisdiction. Failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval elsewhere. Failure to obtain marketing authorization for our product candidates will result in our being unable to market and sell such products. If we fail to obtain approval in any jurisdiction, the geographic market for our product candidates could be limited. Similarly, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates or may grant approvals for more limited patient populations than requested.

Even if we eventually complete clinical testing and receive approval of an NDA or foreign marketing application for our product candidates, the FDA or the applicable foreign regulatory agency may grant approval contingent on the performance of costly additional clinical trials, including Phase 4 clinical trials or the implementation of a Risk Evaluation and Mitigation Strategy ("REMS") which may be required to ensure safe use of the drug after approval. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of that product candidate and would adversely impact our business and prospects.

***Our product candidates may fail to demonstrate safety and efficacy in clinical trials, or may cause serious adverse or unacceptable side effects that could prevent or delay regulatory approval and commercialization, limit the commercial profile of an approved label, increase our costs, necessitate the abandonment or limitation of the development of some of our product candidates or result in significant negative consequences following marketing approval, if any.***

Before obtaining regulatory approvals for the commercial sale of our product candidates, we must demonstrate through lengthy, complex and expensive preclinical 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 efficacy or safety of the product candidate studied for the target indication.

For example, in its Phase 2b clinical trial, rimegepant dosed at 75 mg showed statistically significant improvement as compared to placebo on all four key migraine symptoms—pain, nausea, photophobia, phonophobia—which are inherently subjective endpoints that are difficult to measure. Patients in the trial were provided with an electronic data capturing device, or an electronic subject diary, which they used to record and rank their assessments of pain, nausea, photophobia and phonophobia at specified time points after they had taken the study medication following the occurrence of a migraine attack with moderate to severe pain intensity. The measurements from the trial were based on subjective patient feedback as recorded on their electronic subject diary, which can be influenced by factors outside of our control, and can vary widely from day to day for a particular patient, and from patient to patient and site to site within a clinical trial. The placebo effect also tends to have a more significant impact on clinical trials involving subjective measures such as pain. In our three completed Phase 3 clinical trials, although rimegepant met the co-primary efficacy endpoints of all three trials, we did not achieve statistically significant improvements. as compared to placebo, on the symptom of nausea, which was a secondary efficacy endpoint of the trials.

Moreover, undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label, the limitation of commercial potential or the delay or denial of regulatory approval by the FDA. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Accordingly, we may need to abandon their development or limit development to certain uses or sub-populations in which such side effects are less prevalent, less severe or more acceptable from a risk-benefit perspective. Prior to any regulatory approval of rimegepant, we would need to complete a 12-month safety study as well as longer-term nonclinical toxicology and carcinogenicity studies. If any of these studies identify safety issues, we may need to complete additional studies, or abandon development of rimegepant. Many compounds that initially showed promise in preclinical or early-stage testing have later been found to cause side effects that restricted their use and prevented further development of the compound in the tested indication.

In animal studies, at very high doses, rimegepant was observed to have a negative effect on the liver. We observed elevated liver enzymes in one patient that received very high doses of rimegepant in a drug-drug interaction study and in the completed Phase 2b trial of rimegepant conducted by BMS, one patient dosed with rimegepant experienced an asymptomatic and mild increase in certain hepatic enzymes, which are a type of liver enzyme measured in a liver function test to detect damage and inflammation to the liver. In our recently completed Phase 3 clinical trials of rimegepant, we did not observe any instances of liver enzyme elevations that exceeded the level that is considered by the FDA to be a potentially meaningful indicator of severe

drug-induced liver injury. However, we cannot guarantee that these safety and tolerability results will be replicated in our long-term safety study described below, and it is possible that rimegepant may be observed to cause unacceptable levels of adverse effects or serious adverse effects.

In addition, at our end of Phase 2 meeting, the FDA stated its desire to see a safety study in which patients received daily or near-daily dosing of rimegepant for at least three months. This desire stems from the FDA's concern about a potential liver signal with the class of CGRP antagonists. The FDA stated that any risk of liver injury has to be very low and that exposure with the drug has to be sufficient to cap the risk of liver injury at a level acceptable for the migraine population. We believe the design of our long-term safety study may adequately address this concern by providing for the enrollment of approximately 600 patients who experience eight or more migraine days per month, who will, in the study, be allowed to use rimegepant on a daily basis, which we believe will generate safety data with respect to long-term, frequent use of rimegepant. However, the FDA may determine that our trial design or the data we collect is insufficient to address their concerns, in which case we could be required to conduct additional trials.

Occurrence of serious treatment-related side effects could impede subject recruitment and clinical trial enrollment or the ability of enrolled patients to complete the trial, require us to halt the clinical trial, and prevent receipt of regulatory approval from the FDA. They could also adversely affect physician or patient acceptance of our product candidates or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

***If any of our product candidates receives marketing approval and we, or others, later discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, our ability to market the drug could be compromised.***

Clinical trials of our product candidates are conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If one or more of our product candidates receives regulatory approval, and we, or others, later discover that they are less effective than previously believed, or cause undesirable side effects, a number of potentially significant negative consequences could result, including:

- withdrawal or limitation by regulatory authorities of approvals of such product;
- seizure of the product by regulatory authorities;
- recall of the product;
- restrictions on the marketing of the product or the manufacturing process for any component thereof;
- requirement by regulatory authorities of additional warnings on the label, such as a "black box" warning or contraindication;
- requirement that we implement a REMS or create a medication guide outlining the risks of such side effects for distribution to patients;
- commitment to expensive additional safety studies prior to approval or post-marketing studies required by regulatory authorities of such product;
- commitment to expensive post-marketing studies as a prerequisite of approval by regulatory authorities of such product;
- the product may become less competitive;
- initiation of regulatory investigations and government enforcement actions;
- initiation of legal action against us to hold us liable for harm caused to patients; and
- harm to our reputation and resulting harm to physician or patient acceptance of our products.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, financial condition, and results of operations.

***Our clinical drug development program may not uncover all possible adverse events that patients who use our products may experience. The number of subjects exposed to treatment and the average exposure time in the clinical development program may be inadequate to detect rare adverse events, or chance findings, that may only be detected once our products are administered to more patients and for greater periods of time.***

Clinical trials by their nature utilize a sample of the potential patient population. However, with a limited number of subjects and limited duration of exposure, rare and severe side effects of our product candidates may only be uncovered when a significantly larger number of patients are exposed to the product.

Although we have monitored the subjects in our studies for certain safety concerns and we have not seen evidence of significant safety concerns in our clinical trials, patients treated with our product candidates, if approved, may experience adverse reactions. If safety problems occur or are identified after one of our products reaches the market, the FDA or comparable foreign regulatory authorities may require that we amend the labeling of our product, recall our product, or even withdraw approval for our product. Series adverse events deemed to be caused by our product candidates, either before or after receipt of marketing approval, could have a material adverse effect on the development of our drug candidates and our business as a whole.

***We depend on enrollment of patients in our clinical trials for our product candidates. If we are unable to enroll patients in our clinical trials, our research and development efforts could be adversely affected.***

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. Successful and timely completion of clinical trials will require that we enroll a sufficient number of patients who remain in the trial until its conclusion. If we are unable to enroll a sufficient number of patients in our clinical trials, our timelines for recruiting patients, conducting clinical trials and obtaining regulatory approval of potential products may be delayed. These delays could result in increased costs, delays in advancing our product development, delays in testing the effectiveness of our technology or termination of our clinical trials altogether. We cannot predict how successful we will be at enrolling patients in future clinical trials. Patient enrollment is affected by other factors including:

- the eligibility criteria for the trial in question;
- the perceived risks and benefits of the product candidate in the trial;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating or drugs that may be used off-label for these indications;
- the size of the patient population required for analysis of the trial's primary endpoints;
- competition for patients for competitive product candidates undergoing clinical trials;
- the efforts to facilitate timely enrollment in clinical trials;
- the design of the trial;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- the risk that patients enrolled in clinical trials will drop out of the trials before completion;
- the ability to obtain and maintain patient consents;
- the number of patients with the indication being studied; and
- the proximity and availability of clinical trial sites for prospective patients.

In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors.

Delays in the completion of any clinical trial of our product candidates will increase our costs, slow down our product candidate development and approval process, and delay or potentially jeopardize our ability to commence product sales and generate revenue. In addition, many of the factors that may lead to a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

***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.***

We have limited financial and managerial resources. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Under the Funding Agreement, we are obligated to take certain steps to complete clinical trials and commercialize products containing the compounds rimegepant or BHV-3500 and certain derivative compounds thereof. These obligations could adversely impact or delay our ability to develop other product candidates. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products 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 royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

***We may become exposed to costly and damaging liability claims, either when testing our product candidates in the clinic or at the commercial stage, and our product liability insurance may not cover all damages from such claims.***

We are exposed to potential product liability and professional indemnity risks that are inherent in the research, development, manufacturing, marketing, and use of pharmaceutical products. We currently have no products that have been approved for commercial sale. However, the current and future use of product candidates by us in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims might be made by patients that use the product, healthcare providers, pharmaceutical companies, or others selling such products. In addition, we have agreed to indemnify the licensors of the intellectual property related to our product candidates against certain intellectual property infringement claims. Any claims against us, or with respect to which we are obligated to provide indemnification, regardless of their merit, could be difficult and costly to defend or settle, and could compromise the market acceptance of our product candidates or any prospects for commercialization of our product candidates, if approved.

Although the clinical trial process is designed to identify and assess potential side effects, it is always possible that a drug, even after regulatory approval, may exhibit unforeseen side effects. If any of our product candidates were to cause adverse side effects during clinical trials or after approval of the product candidate, we may be exposed to substantial liabilities. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use our product candidates.

Although we maintain product liability insurance coverage, such insurance may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage each time we commence a clinical trial and if we successfully commercialize any product candidate. As the expense of insurance coverage is increasing, we may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. If a successful product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

***If serious adverse events or other undesirable side effects are identified during the use of our product candidates in investigator-sponsored trials, it may adversely affect our development of such product candidates.***

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt nonclinical studies and clinical trials, or could make it more difficult for us to enroll patients in our clinical trials. If serious adverse events or other undesirable side effects or unexpected characteristics of our product candidates are observed in investigator-sponsored trials, further clinical development of such product candidate may be delayed or we may not be able to continue development of such product candidate at all, and the occurrence of these events could have a material adverse effect on our business. Undesirable side effects caused by our product candidates could also result in the delay or denial of regulatory approval by the FDA or other regulatory authorities or in a more restrictive label than we expect.

***The currently reported results of our Zydis ODT Phase 3 trial of rimegepant are based on topline data for the trial and may differ from complete trial results once additional data are received and evaluated. Also, our long-term safety study of rimegepant is ongoing and could result in adverse safety data in the future. In addition, the FDA may disagree with the interpretation of the results of, or the sufficiency of the data from our clinical trials of rimegepant. There can be no assurance that our NDAs for rimegepant will be submitted in the time frame that we anticipate or that, if accepted for review, the NDAs will be approved by the FDA.***

The reported results of our ODT Phase 3 trial of rimegepant consist of only topline data on the co-primary endpoints and certain secondary endpoints as well as safety and tolerability data. Topline data are based on a preliminary analysis of currently available efficacy and safety data, and therefore these results are subject to change following a comprehensive review of the more extensive data we expect to receive when available. These data are based on important assumptions, estimations, calculations and information currently available to us, and we have not received or had an opportunity to evaluate all of the data from this trial, including data with respect to all of the secondary and other endpoints from this trial. As a result, we may have additional, different or conclusions that may qualify the topline results, once the complete data have been received and fully evaluated.

In addition, we cannot be certain that we will submit our NDAs for rimegepant to the FDA within the timeframe we currently expect. Additionally, while we currently intend to submit the initial NDAs for the Zydis ODT formulation and the tablet formulation concurrently, we cannot be certain whether the NDAs we submit will be submitted concurrently. Prior to submitting any NDA, in addition to completing our analysis of the data from the Zydis ODT trial and the data from our ongoing long-term safety study of rimegepant, we also must provide information relating to the manufacture of rimegepant and other modules of any NDA. In addition, our long-term safety study is ongoing and there can be no assurance that we will not receive adverse safety data from this study in the future. In addition, there can be no assurance that the FDA will agree with our

conclusions or the conclusions of our investigators or independent liver panel with the regard to whether the adverse events observed in the clinical trials were related to rimegepant or with regard to the safety data generally. For example, the FDA has indicated its desire to see data from our safety study in which patients receive daily or near-daily dosing of rimegepant, but did not specify how much data would be sufficient. While we have designed our long-term safety study of rimegepant to generate this data, there can be no assurance that a sufficient number of patients in the trial have taken or will take rimegepant frequently enough to adequately address the FDA's request.

If any of the additional information we must generate is not positive or is delayed or if future safety data from our ongoing long-term safety study is not positive, we may not be able to submit any of our NDAs for rimegepant within the timeframe we currently anticipate or at all. There also can be no assurance that once submitted, the FDA will accept any of our NDAs for filing and review.

Even if our NDAs are accepted by the FDA for review, clinical trial results and other aspects of the information in our NDAs will be subject to interpretation and we cannot be certain that the clinical trial results and other information in our NDAs for rimegepant will be sufficient to support approval of the NDAs. Among other things, the FDA may, despite prior published guidance and advice, decide that the clinical and non-clinical data from our rimegepant development program are not sufficient to support regulatory approval.

If we are unable to obtain or are delayed in obtaining FDA approval for rimegepant it would materially adversely affect our business, financial condition, results of operations and prospects and the value of our common shares.

**Risks Related to Commercialization of Our Product Candidates**

***We have never commercialized a product candidate and we may lack the necessary expertise, personnel and resources to successfully commercialize any of our products that receive regulatory approval on our own or together with collaborators.***

We have never commercialized a product candidate. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, acquiring the rights to our product candidates and undertaking preclinical studies and clinical trials of our product candidates. We currently have no sales force, marketing or distribution capabilities. To achieve commercial success of our product candidates, if any are approved, we will have to develop our own sales, marketing and supply capabilities or outsource these activities to a third party.

Factors that may affect our ability to commercialize our product candidates on our own include recruiting and retaining adequate numbers of effective sales and marketing personnel, obtaining access to or persuading adequate numbers of physicians to prescribe our product candidates and other unforeseen costs associated with creating an independent sales and marketing organization. Developing a sales and marketing organization requires significant investment, is time-consuming and could delay the launch of our product candidates. We may not be able to build an effective sales and marketing organization in the United States, the European Union or other key global markets. If we are unable to build our own distribution and marketing capabilities or to find suitable partners for the commercialization of our product candidates, we may have difficulties generating revenue from them.

***We operate in a highly competitive and rapidly changing industry.***

Biopharmaceutical product development is highly competitive and subject to rapid and significant technological advancements. Our success is highly dependent upon our ability to in-license, acquire, develop and obtain regulatory approval for new and innovative products on a cost-effective basis and to market them successfully. In doing so, we face and will continue to face intense competition from a variety of businesses, including large, fully integrated, well-established pharmaceutical companies who already possess a large share of the market, specialty pharmaceutical and biopharmaceutical companies, academic institutions, government agencies and other private and public research institutions in the United States, the European Union and other jurisdictions.

With respect to our CGRP receptor antagonists, rimegepant and BHV-3500, we face competition from other companies that market or are developing migraine treatments. These include products in the class of products known as triptans, including the 5-HT1F receptor antagonist lasmiditan being developed by Eli Lilly and Company, as well as other small molecule CGRP receptor antagonists such as ubrogepant, which has completed Phase 3 trials, and atogepant in Phase 3 clinical trials, being developed by Allergan. It is anticipated that NDAs for lasmiditan and ubrogepant will likely be submitted to the FDA prior to when we expect to submit an NDA for rimegepant. Our other CGRP product candidate, BHV-3500, is in an earlier stage of development than ubrogepant, lasmiditan, atogepant and rimegepant. These other products are more advanced in their clinical development than rimegepant and BHV-3500, and therefore may receive marketing approval before our migraine product candidates receive marketing approval, if at all, which could make it more difficult for our products to achieve commercially reasonable market acceptance. In addition, with the recent approval by the FDA of three biologic CGRP receptor binding monoclonal antibodies, of Aimovig (Amgen/Novartis), Ajovy (Teva), and Emgality (Lilly) for the preventive treatment of migraine in adults. The market opportunity for rimegepant for the acute treatment of migraine may decrease if the antibodies

are successful in preventing migraine in patients. Wide adoption of Aimovig, Emgality and/or Ajovy may also cause clinicians to be more hesitant in prescribing an oral CGRP for acute treatment in a patient who is receiving a biologic CGRP for prevention. Finally, as acute treatment of migraine moves from a relatively generic market to a branded market, it is anticipated that payers will implement new or more stringent prior authorization procedures, such as step therapy in which a patient must try a less expensive drug first, for patients to receive these newer and more expensive medications, thereby potentially slowing new product uptake and adoption.

With respect to BHV-0223, which we are developing for the treatment of ALS, we believe our primary competition is Covis Pharmaceuticals, which sells Rilutek, the brand name for riluzole, and the six approved generic versions of Rilutek. Edaravone (Radicava, Mitsubishi Tanabe Pharma) has been approved by the FDA for the treatment of ALS, based on efficacy studies conducted in Japan, with the vast majority of patients on background riluzole therapy. Edaravone is administered to patients by intravenous infusion. We are aware of at least two other company planning to market a new formulation of riluzole. Aquestive Therapeutics, Inc. (previously called MonoSol Rx) has filed an IND with the FDA to conduct clinical trials for a riluzole oral soluble film and has received orphan drug designation. Aquestive Therapeutics, Inc. has publicly announced they plan to file an NDA for a riluzole oral soluble film in 2019. Italfarmaco SpA, or Italfarmaco, a private Italian company, markets an oral liquid suspension formulation of riluzole in the United Kingdom and elsewhere in Europe under the brand name Teglutik. Tiglutik. the US brand name for Italfarmaco's oral liquid suspension formulation of riluzole was approved for marketing in the United States in September 2018. To our knowledge based on publicly available information, no other companies are marketing sublingual formulations of riluzole. Other companies of which we are not aware may also be developing formulations using riluzole; if such companies pursued regulatory approval of such product candidates using the Section 505(b)(2) regulatory pathway, those product candidates would potentially compete with BHV-0223. For example, Italfarmaco has obtained orphan designation for Tiglutik and Aquestive Therapeutics has obtained orphan drug designation for its oral soluble film product candidate, and these companies are eligible to obtain orphan exclusivity subject to a showing of clinical superiority to riluzole. If Tiglutik is shown to be clinically superior to Rilutek and is granted orphan exclusivity, then BHV-0223 would need to demonstrate clinical superiority to Tiglutik in order to receive marketing approval. Additionally, if the oral soluble film being developed by Aquestive Therapeutics is shown to be clinically superior to Rilutek and also receives marketing approval before BHV-0223, then BHV-0223 would need to demonstrate clinical superiority to such agents in order to receive marketing approval. If we expand our development of BHV-0223 into additional neuropsychiatric or other indications, we would face substantial competition from companies that develop or sell products that treat those indications.

With respect to troriluzole, which we are currently developing for the treatment of ataxias and other neurologic disorders, with SCA as our initial indication, there are currently no approved drug treatments for spinocerebellar ataxias in the United States. We are also developing troriluzole for the potential treatment of Alzheimer's disease, OCD and GAD and if we continue to pursue those indications, we would face substantial competition from companies that develop or sell products that treat Alzheimer's disease, OCD or GAD. With respect to BHV-5000, which we are developing for the treatment of neuropsychiatric conditions the market size and competition will depend on each indication. For example, indications such as CRPS and Rett syndrome have limited treatment options while other indications, such as depression, have multiple approved treatments.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Mergers and acquisitions in the biopharmaceutical industry could result in even more resources being concentrated among a small number of our competitors.

Competition may further increase as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing, on an exclusive basis, products that are more effective or less costly than any product candidate that we may develop.

Established biopharmaceutical companies may invest heavily to accelerate research and development of novel compounds or to in-license novel compounds that could make our product candidates less competitive. 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. Accordingly, our competitors may succeed in obtaining patent protection, discovering, developing, receiving FDA approval for or commercializing drugs before we do, which would have an adverse impact on our business and results of operations.

The availability of our competitors' products could limit the demand and the price we are able to charge for any product candidate we commercialize, if any. The inability to compete with existing or subsequently introduced drugs would harm our business, financial condition and results of operations.

***The successful commercialization of certain of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage, reimbursement levels and pricing policies. Failure to obtain or maintain adequate coverage and reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.***

The availability and adequacy of coverage and reimbursement by governmental healthcare programs, such as Medicare and Medicaid, private health insurers and other third-party payors, is essential for most patients to be able to afford products such as our product candidates, if approved. Our ability to achieve acceptable levels of coverage and reimbursement for products by third-party payors will have an effect on our ability to successfully commercialize our product candidates, if approved, and attract additional collaboration partners to invest in the development of our product candidates. Coverage under certain government programs, such as Medicare, Medicaid and Tricare, may not be available for certain of our product candidates. 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. We cannot be sure that coverage and adequate reimbursement in the United States, the European Union or elsewhere will be available for any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs when an equivalent generic drug or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidates as substitutable by less expensive therapies and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy or improved convenience of administration with our product candidates, pricing of existing drugs may limit the amount we will be able to charge for our product candidates, once approved. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in product development. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates, and may not be able to obtain a satisfactory financial return on products that we may develop.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, third-party payors, including private and governmental programs, play an important role in determining the extent to which new drugs and biologics will be covered. The Medicare and Medicaid programs increasingly are used as models for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. Some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse health care providers who use such therapies. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

Obtaining and maintaining reimbursement status is time-consuming and costly. No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for 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. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases at short notice, and we believe that changes in these rules and regulations are likely.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. The continuing efforts of the government, insurance companies, managed care organizations and other payors of health care services to contain or reduce costs of health care may adversely affect:

- the demand for any products for which we may obtain regulatory approval;
- our ability to set a price that we believe is fair for our products;
- our ability to obtain coverage and adequate reimbursement approval for a product;
- our ability to generate revenues and achieve or maintain profitability; and
- the level of taxes that we are required to pay.

***Even if we obtain regulatory approval for our product candidates, they will remain subject to ongoing regulatory oversight.***

Even if we obtain regulatory approval for any of our product candidates, they will be subject to extensive and ongoing regulatory requirements for manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, sampling and record-keeping. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with current good manufacturing practices ("cGMP") regulations and good clinical practices, or GCPs, for any clinical trials that we conduct post-approval, all of which may result in significant expense and limit our ability to commercialize such products. In addition, any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require a REMS as a condition of approval of our product candidates, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools.

The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. 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 we may not achieve or sustain profitability. Moreover, if there are changes in the application of legislation or regulatory policies, or if problems are discovered with a product or our manufacture of a product, or if we or one of our distributors, licensees or co-marketers fails to comply with regulatory requirements, the regulators could take various actions. These include:

- issuing warning or untitled letters;
- seeking an injunction or imposing civil or criminal penalties or monetary fines;
- suspension or imposition of restrictions on operations, including product manufacturing;
- seizure or detention of products, refusal to permit the import or export of products, or requesting that we initiate a product recall;
- suspension or withdrawal of our marketing authorizations;
- suspension of any ongoing clinical trials;
- refusal to approve pending applications or supplements to applications submitted by us; or
- requiring us to conduct additional clinical trials, change our product labeling or submit additional applications for marketing authorization.

Moreover, the FDA strictly regulates the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant civil, criminal and administrative penalties.

If any of these events occurs, our ability to sell such product may be impaired, and we may incur substantial additional expense to comply with regulatory requirements, which could adversely affect our business, financial condition and results of operations.

***Even if any of our product 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.***

Even if the FDA approves the marketing of any product candidates that we develop, physicians, patients, third-party payors or the medical community may not accept or use them. Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. If any of our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenue or any profits from operations. The degree of market acceptance of our product candidates that are approved for commercial sale will depend on a variety of factors, including:

- the efficacy and potential advantages compared to alternative treatments;
- effectiveness of sales and marketing efforts;
- the cost of treatment in relation to alternative treatments, including any similar generic treatments;
- our ability to offer our products, if approved, for sale at competitive prices;

- 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 marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement, and patients' willingness to pay out-of-pocket in the absence of third-party coverage or adequate reimbursement;
- the prevalence and severity of any side effects;
- any restrictions on the use of our products, if approved, together with other medications; and
- other potential advantages over alternative treatment methods.

Our efforts to educate physicians, patients, third-party payors and others in the medical community on the benefits of our products, if approved, may require significant resources and may never be successful. Such efforts may require more resources than are typically required due to the complexity and uniqueness of our product candidates. Because we expect sales of our product candidates, if approved, to generate substantially all of our product revenue for the foreseeable future, the failure of our product candidates to find market acceptance would harm our business and could require us to seek additional financing.

In addition, the potential market opportunity for our product candidates is difficult to estimate precisely. Our estimates of the potential market opportunity are predicated on several key assumptions such as industry knowledge and publications, third-party research reports and other surveys. While we believe that our internal assumptions are reasonable, these assumptions may be inaccurate. If any of the assumptions proves to be inaccurate, then the actual market for our product candidates could be smaller than our estimates of the potential market opportunity. If the actual market for our product candidates is smaller than we expect, or if the products fail to achieve an adequate level of acceptance by physicians, health care payors and patients, our revenue from product sales may be limited and we may be unable to achieve or maintain profitability.

***We currently have limited marketing, sales or distribution infrastructure. If we are unable to develop sales, marketing and distribution capabilities on our own or through collaborations, or if we fail to achieve adequate pricing or reimbursement we will not be successful in commercializing our product candidates, if approved.***

We currently have limited marketing, sales and distribution capabilities and our product candidates are still in clinical development. If any of our product candidates are approved, we intend either to establish a sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize our product candidates, or to outsource these functions to a third party. Either of these options would be expensive and time-consuming. These costs may be incurred in advance of any approval of our product candidates. In addition, we may not be able to hire a sales force that is sufficient in size or has adequate expertise in the medical markets that we intend to target. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of our products.

To the extent that we enter into collaboration agreements with respect to marketing, sales or distribution, our product revenue may be lower than if we directly marketed or sold any approved products. In addition, any revenue we receive will depend in whole or in part upon the efforts of these third-party collaborators, which may not be successful and are generally not within our control. If we are unable to enter into these arrangements on acceptable terms or at all, we may not be able to successfully commercialize any approved products. If we are not successful in commercializing any approved products, 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.

***If the FDA or comparable foreign regulatory authorities approve generic versions of any of our products that receive marketing approval, or such authorities do not grant our products appropriate periods of exclusivity before approving generic versions of our products, the sales of our products could be adversely affected.***

Once an NDA is approved, the product covered thereby becomes a "reference listed drug" in the FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," commonly known as the Orange Book. Manufacturers may seek approval of generic versions of reference listed drugs through submission of abbreviated new drug applications ("ANDAs") in the United States. In support of an ANDA, a generic manufacturer need not conduct clinical trials. Rather, the applicant generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labeling as the reference listed drug and that the generic version is bioequivalent to the reference listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference listed drug and companies that produce generic products are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference listed drug is typically lost to the generic product.

The FDA may not approve an ANDA for a generic product until any applicable period of non-patent exclusivity for the reference listed drug has expired. The FDCA provides a period of five years of non-patent exclusivity for a new drug containing

a new chemical element ("NCE"). Specifically, in cases where such exclusivity has been granted, an ANDA may not be submitted to the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the reference listed drug is either invalid or will not be infringed by the generic product, in which case the applicant may submit its application four years following approval of the reference listed drug.

While we believe that rimegepant contains active ingredients that would be treated as NCEs by the FDA and, therefore, if approved, should be afforded five years of data exclusivity, the FDA may disagree with that conclusion and may approve generic products after a period that is less than five years. Moreover, while we believe that troriluzole, a prodrug of riluzole, and BHV-5000. will also be treated as NCEs under current FDA interpretations, if approved, the FDA may ultimately disagree with our conclusion. Manufacturers may seek to launch these generic products following the expiration of the applicable marketing exclusivity period, even if we still have patent protection for our product.

Competition that our products may face from generic versions of our products could materially and adversely impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made in those product candidates.

**Risks Related to Our Dependence on Third Parties**

***If we fail to comply with our obligations under our existing and any future intellectual property licenses with third parties, we could lose license rights that are important to our business.***

We are party to several license agreements under which we in-license patent rights and other intellectual property related to our business, including a license agreement with BMS, under which we were granted an exclusive license relating to rimegepant and BHV-3500, a license agreement with ALS Biopharma and Fox Chase Chemical Diversity Center, Inc., pursuant to which we were assigned intellectual property rights relating to troriluzole, a license agreement with Catalent, pursuant to which we were granted an exclusive license to use their Zydis technology in the development of BHV-0223 and rimegepant, license agreements with AstraZeneca, pursuant to which we were granted exclusive licenses relating to BHV-5000 and verdiperstat.

We have also entered into other license agreements that relate to other patent rights and other indications we are pursuing or may pursue in the future. We may enter into additional license agreements in the future. Our license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. Any uncured, material breach under these license agreements could result in our loss of rights to practice the patent rights and other intellectual property licensed to us under these agreements, and could compromise our development and commercialization efforts for our product candidates.

***Our intellectual property in-licenses with third parties may be subject to disagreements over contract interpretations, which could narrow the scope of our rights to the relevant intellectual property or technology or increase our financial or other obligations to our licensors.***

The agreements under which we currently in-license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could harm our business, financial condition, results of operations and prospects. If any of our current or future licenses or material relationships or any in-licenses upon which our current or future product candidates are based are terminated or breached, we may:

- lose our rights to develop and market our product candidates;
- lose patent protection for our product candidates;
- experience significant delays in the development or commercialization of our product candidates;
- not be able to obtain any other licenses on acceptable terms, if at all; or
- incur liability for damages.

If we experience any of the foregoing, it could harm our business, financial condition and results of operations.

***We rely on third parties to conduct our preclinical studies and clinical trials and if these third parties perform in an unsatisfactory manner, our business could be substantially harmed.***

We have historically conducted, and we intend to continue to conduct our clinical trials, using our own clinical resources, while also leveraging expertise and assistance from contract research organizations ("CROs") as appropriate. We do not

currently have the ability to independently conduct large-scale clinical trials, such as a Phase 3 clinical trial, without outside assistance.

We have relied upon and plan to continue to rely upon medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct or assist us in conducting GCP-compliant clinical trials on our product candidates properly and on time, and may not currently have all of the necessary contractual relationships in place to do so. Once we have established contractual relationships with such third-party CROs, we will have only limited control over their actual performance of these activities.

We and our CROs and other vendors are required to comply with cGMP, GCP and good laboratory practices ("GLP"), which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Union and any comparable foreign regulatory authorities for all of our product candidates in preclinical and clinical development. Regulatory authorities enforce these regulations through periodic inspections of trial sponsors, principal investigators, clinical trial sites and other contractors. Although we rely on CROs to conduct any current or planned GLP-compliant preclinical studies and GCP-compliant clinical trials and have limited influence over their actual performance, we remain responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with its investigational plan and protocol and applicable laws and regulations, and our reliance on the CROs does not relieve us of our regulatory responsibilities. If we or any of our CROs or vendors fail to comply with applicable regulations, the data generated in our preclinical studies and clinical trials may be deemed unreliable and the FDA, EMA or any comparable foreign regulatory agency may require us to perform additional preclinical studies and clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory agency, such regulatory agency will determine that all of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with products produced under cGMP requirements. Our failure to comply with these requirements may require us to repeat clinical trials, which would delay the regulatory approval process.

While we will have agreements governing their activities, our CROs will not be our employees, and we will not be able to control whether or not they devote sufficient time and resources to our future preclinical and 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 which could harm our business. We face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs, which may reduce our trade secret protection and allow our potential competitors to access and exploit our proprietary technology. If our CROs do not successfully carry out their contractual duties or obligations, fail to 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 or regulatory requirements or for any other reason, our clinical trials may be extended, delayed or terminated, the clinical data generated in our clinical trials may be deemed unreliable, and we may not be able to obtain regulatory approval for, or successfully commercialize any product candidate that we develop. As a result, our financial results and the commercial prospects for any product candidate that we develop would be harmed, our costs could increase, and our ability to generate revenue could be delayed.

If our relationship with these CROs terminates, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. Switching or adding additional CROs involves substantial cost and requires management time and focus, and could delay development and commercialization of our product candidates. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can negatively impact our ability to meet our desired clinical development timelines. Though we intend to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a negative impact on our business and financial condition.

***We currently rely on third parties for the production of our clinical supply of our product candidates and we intend to continue to rely on third parties for our clinical and commercial supply.***

We currently rely on and expect to continue to rely on third parties for the manufacturing and supply of chemical compounds for the clinical trials of our product candidates and, if approved, our commercial supply. Reliance on third-party suppliers may expose us to different risks than if we were to manufacture product candidates ourselves. The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA or other regulatory authorities pursuant to inspections that will be conducted after we submit our NDA or comparable foreign marketing application to the FDA or other foreign regulatory agency.

Although we have auditing rights with all our manufacturing counterparties, we do not have control over a supplier’s or manufacturer’s compliance with these laws, regulations and applicable cGMP standards and other laws and regulations, such as those related to environmental health and safety matters. There can be no assurance that our preclinical and clinical development product supplies will not be limited, interrupted or of satisfactory quality or continue to be available at acceptable prices. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure or maintain regulatory approval for their

manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. In the event that any of our manufacturers fails to comply with regulatory requirements or to perform its obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, or if the FDA or a comparable foreign regulatory agency 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. Any replacement of our manufacturers could require significant effort, time and expense, which could significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

Any failure to achieve and maintain compliance with these laws, regulations and standards could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical trials of our product candidates under development;
- delay in submitting regulatory applications, or receiving regulatory approvals, for our product candidates;
- subjecting third-party manufacturing facilities or our own facilities to additional inspections by regulatory authorities;
- requirements to cease distribution or to recall batches of our product candidates;
- suspension of manufacturing of our product candidates;
- revocation of obtained approvals; and
- inability to meet commercial demands for our product candidates in the event of approval.

Furthermore, third-party providers may breach agreements they have with us because of factors beyond our control. They may also terminate or refuse to renew their agreements because of their own financial difficulties or business priorities, potentially at a time that is costly or otherwise inconvenient for us. If we were unable to find adequate replacement or another acceptable solution in time, our clinical trials could be delayed or our commercial activities could be harmed.

In addition, the fact that we are dependent on third parties for the manufacture, storage and distribution of our product candidates means that we are subject to the risk that our product candidates and, if approved, commercial products may have manufacturing defects that we have limited ability to prevent or control. The sale of products containing such defects could result in recalls or regulatory enforcement action that could adversely affect our business, financial condition and results of operations. Our reliance on third parties also exposes us to the possibility that they, or third parties with access to their facilities, will have access to and may appropriate our trade secrets or other proprietary information.

***We rely completely on third-party contractors to supply, manufacture and distribute clinical drug supplies for our product candidates, including certain sole-source suppliers and manufacturers; we intend to rely on third parties for commercial supply, manufacturing and distribution if any of our product candidates receive regulatory approval; and we expect to rely on third parties for supply, manufacturing and distribution of preclinical, clinical and commercial supplies of any future product candidates.***

We do not currently have, nor do we plan to acquire, the internal infrastructure or capability to supply, manufacture or distribute preclinical, clinical or commercial quantities of drug substances or products.

Our ability to develop our product candidates depends and our ability to commercially supply our products will depend, in part, on our ability to successfully obtain the active pharmaceutical ingredients ("APIs") and other substances and materials used in our product candidates from third parties and to have finished products manufactured by third parties in accordance with regulatory requirements and in sufficient quantities for preclinical and clinical testing and commercialization. If we fail to develop and maintain supply relationships with these third parties, we may be unable to continue to develop or commercialize our product candidates.

We do not have direct control over the ability of our contract suppliers and manufacturers to maintain adequate capacity and capabilities to serve our needs, including quality control, quality assurance and qualified personnel. Although we are ultimately responsible for ensuring compliance with regulatory requirements such as cGMPs, we are dependent on our contract suppliers and manufacturers for day-to-day compliance with cGMPs for production of both APIs and finished products. Facilities used by our contract suppliers and manufacturers to produce the APIs and other substances and materials or finished products for commercial sale must pass inspection and be approved by the FDA and other relevant regulatory authorities. Our contract suppliers and manufacturers must comply with cGMP requirements enforced by the FDA through its facilities inspection program and review of submitted technical information. If the safety of any product or product candidate or component is compromised due to a failure to adhere to applicable laws or for other reasons, we may not be able to successfully commercialize or obtain regulatory approval for the affected product or product candidate, and we may be held liable for injuries sustained as a result. Any of these factors could cause a delay or termination of preclinical studies, clinical trials or

regulatory submissions or approvals of our product candidates, and could entail higher costs or result in our being unable to effectively commercialize our approved products on a timely basis, or at all.

We also rely and will continue to rely on certain third parties as the sole source of the materials they supply or the finished products they manufacture. For example, Catalent is the sole-source supplier for the Zydis formulation of BHV-0223, and the ODT formulation of rimegepant. We may also have sole-source suppliers for one or more of our other product candidates. Some of the APIs and other substances and materials used in our product candidates are currently available only from one or a limited number of domestic or foreign suppliers and foreign manufacturers and certain of our finished product candidates are manufactured by one or a limited number of contract manufacturers. In the event an existing supplier fails to supply product on a timely basis or in the requested amount, supplies product that fails to meet regulatory requirements, becomes unavailable through business interruption or financial insolvency or loses its regulatory status as an approved source or if we or our manufacturers are unable to renew current supply agreements when such agreements expire and we do not have a second supplier, we likely would incur added costs and delays in identifying or qualifying replacement manufacturers and materials and there can be no assurance that replacements would be available to us on a timely basis, on acceptable terms or at all. In certain cases we may be required to get regulatory approval to use alternative suppliers, and this process of approval could delay production of our products or development of product candidates indefinitely. We and our manufacturers do not currently maintain inventory of these APIs and other substances and materials. Any interruption in the supply of an API or other substance or material or in the manufacture of a finished product could have a material adverse effect on our business, financial condition, operating results and prospects.

In addition, these contract manufacturers are or may be engaged with other companies to supply and manufacture materials or products for such companies, which also exposes our suppliers and manufacturers to regulatory risks for the production of such materials and products. As a result, failure to meet the regulatory requirements for the production of those materials and products may also affect the regulatory clearance of a contract supplier's or manufacturer's facility. If the FDA or a comparable foreign regulatory agency does not approve these facilities for the supply or manufacture of our product candidates, or if it withdraws its approval in the future, we may need to find alternative supply or manufacturing facilities, which would negatively impact our ability to develop, obtain regulatory approval of or market our product candidates, if approved.

As we prepare for later-stage clinical trials and potential commercialization, we will need to take steps to increase the scale of production of our product candidates, which may include transferring production to new third-party suppliers or manufacturers. In order to conduct larger or late-stage scale clinical trials for our product candidates and supply sufficient commercial quantities of the resulting drug product and its components, if that product candidate is approved for sale, our contract manufacturers and suppliers will need to produce our product candidates in larger quantities, more cost effectively and, in certain cases, at higher yields than they currently achieve. These third-party contractors may not be able to successfully increase the manufacturing capacity for any of such product candidates in a timely or cost-effective manner or at all. Significant scale up of manufacturing may require additional processes, technologies and validation studies, which are costly, may not be successful and which the FDA and foreign regulatory authorities must review and approve. In addition, quality issues may arise during those scale-up activities because of the inherent properties of a product candidate itself or of a product candidate in combination with other components added during the manufacturing and packaging process, or during shipping and storage of the APIs or the finished product. If our third-party contractors are unable to successfully scale up the manufacture of any of our product candidates in sufficient quality and quantity and at commercially reasonable prices, and we are unable to find one or more replacement suppliers or manufacturers capable of production at a substantially equivalent cost in substantially equivalent volumes and quality, and we are unable to successfully transfer the processes on a timely basis, the development of that product candidate and regulatory approval or commercial launch for any resulting products may be delayed, or there may be a shortage in supply, either of which could significantly harm our business, financial condition, operating results and prospects.

We expect to continue to depend on third-party contract suppliers and manufacturers for the foreseeable future. Our supply and manufacturing agreements, if any, do not guarantee that a contract supplier or manufacturer will provide services adequate for our needs. We and our contract suppliers and manufacturers continue to improve production processes, certain aspects of which are complex and unique, and we may encounter difficulties with new or existing processes. While we attempt to build in certain contractual obligations on such third-party suppliers and manufacturers, we may not be able to ensure that such third parties comply with these obligations. Depending on the extent of any difficulties encountered, we could experience an interruption in clinical or commercial supply, with the result that the development, regulatory approval or commercialization of our product candidates may be delayed or interrupted. In addition, third-party suppliers and manufacturers may have the ability to increase the price payable by us for the supply of the APIs and other substances and materials used in our product candidates, in some cases without our consent.

Additionally, any damage to or destruction of our third-party manufacturers' or suppliers' facilities or equipment may significantly impair our ability to have our product candidates manufactured on a timely basis. Furthermore, if a contract manufacturer or supplier becomes financially distressed or insolvent, or discontinues our relationship beyond the term of any

existing agreement for any other reason, this could result in substantial management time and expense to identify, qualify and transfer processes to alternative manufacturers or suppliers, and could lead to an interruption in clinical or commercial supply.

Our reliance on contract manufacturers and suppliers further exposes us to the possibility that they, or third parties with access to their facilities, will have access to and may misappropriate our trade secrets or other proprietary information.

In addition, the manufacturing facilities of certain of our suppliers are located outside of the United States. This may give rise to difficulties in importing our products or product candidates or their components into the United States or other countries as a result of, among other things, regulatory agency approval requirements or import inspections, incomplete or inaccurate import documentation or defective packaging.

***We, or third-party manufacturers on whom we rely, may be unable to successfully scale-up manufacturing of our product candidates in sufficient quality and quantity, which would delay or prevent us from developing our product candidates and commercializing approved products, if any.***

In order to conduct clinical trials of our product candidates and commercialize any approved product candidates, we, or our manufacturers, will need to manufacture them in large quantities. We, or our manufacturers, may be unable to successfully increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities. If we, or any of our manufacturers, are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing, and clinical trials of that product candidate may be delayed or infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business. If we are unable to obtain or maintain third-party manufacturing for commercial supply of our product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully.

***We may in the future enter into collaborations with third parties to develop our product candidates. If these collaborations are not successful, our business could be harmed.***

We may potentially enter into collaborations with third parties in the future. We will face, to the extent that we decide to enter into collaboration agreements, significant competition in seeking appropriate collaborators. Moreover, collaboration arrangements are complex and time-consuming to negotiate, document, implement and maintain. We may not be successful in our efforts to establish and implement collaborations or other alternative arrangements should we so chose to enter into such arrangements. The terms of any collaborations or other arrangements that we may establish may not be favorable to us.

Any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborations are subject to numerous risks, including:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- the clinical trials conducted as part of these collaborations may not be successful;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for clinical trials, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- we may not have access to, or may be restricted from disclosing, certain information regarding product candidates being developed or commercialized under a collaboration and, consequently, may have limited ability to inform our shareholders about the status of such product candidates;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates developed in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;

- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of any such product candidate;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development of any product candidates, may cause delays or termination of the research, development or commercialization of such product candidates, may lead to additional responsibilities for us with respect to such product candidates or may result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- disputes may arise with respect to the ownership of intellectual property developed pursuant to our collaborations;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

If any such potential future collaborations do not result in the successful development and commercialization of product candidates, or if one of our future collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, the development of our product candidates could be delayed and we may need additional resources to develop our product candidates. In addition, if one of our future collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and the perception of us in the business and financial communities could be adversely affected. All of the risks relating to product development, regulatory approval and commercialization apply to the activities of our potential future collaborators.

***If we are not able to establish or maintain collaborations, we may have to alter some of our future development and commercialization plans.***

Our product development programs and the potential commercialization of our product candidates will require substantial additional capital to fund expenses. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the future development and potential commercialization of those product candidate. Furthermore, we may find that our programs require the use of proprietary rights held by third parties, and the growth of our business may depend in part on our ability to acquire, in-license or use these proprietary rights.

We face significant competition in seeking appropriate collaborators, and a number of more established companies may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, financial resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA, EMA, National Medical Products Administration or similar foreign regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under existing license agreements from entering into agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. Even if we are able to obtain a license to intellectual property of interest, we may not be able to secure exclusive rights, in which case others could use the same rights and compete with us. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to curtail the development of such product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential

commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

***Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.***

Because we rely on third parties to develop and manufacture our product candidates, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets. Despite these contractual agreements with third parties, sharing trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may harm our business.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

**Risks Related to Regulatory Compliance**

***Enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and may affect the prices we may set.***

In the United States, the European Union, and other foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the United States federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, in March 2010, the Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively ACA was enacted, which substantially changes the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include:

- an annual, non-deductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, which is apportioned among these entities according to their market share in certain government healthcare programs;
- a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer and 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- new requirements to report certain financial arrangements with physicians and certain others, including reporting "transfers of value" made or distributed to prescribers and other healthcare providers and reporting investment interests held by physicians and their immediate family members;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- extension of a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;

- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of the Center for Medicare Innovation at the Centers for Medicare and Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, 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 that repealed, 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 on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, or the BBA, among other things, amended the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." On December 14, 2018, a Texas U.S. District Court Judge ruled that the ACA is unconstitutional in its entirety because the “individual mandate” was repealed by Congress as part of the Tax Cuts and Jobs Act of 2017. While the Texas U.S. District Court Judge, as well as the Trump administration and CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the ACA will impact the ACA or our business or financial condition.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation’s automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2027 unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other health care funding, which could have an adverse effect on our customers and accordingly, our financial operations.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS is developing new payment and delivery models, such as bundled payment models. The U.S. Department of Health and Human Services (“HHS”) moved 30% of Medicare payments to alternative payment models tied to the quality or value of services in 2016. Additionally, HHS had set a goal of moving 50% of Medicare payments into these alternative payment models by the end of 2018, but due to a policy shift under the Trump Administration, it is unclear how and when such changes will be implemented. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Further, there have been several recent U.S. congressional inquiries and proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, the Trump Administration’s budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, on May 11, 2018, President Trump laid out his administration’s "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. HHS has already started the process of soliciting feedback on some of these measures and, at the same, is immediately implementing others under its existing authority. For example, in

September 2018, the Center for Medicare and Medicaid Services ("CMS") announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019, and in October 2018, CMS proposed a new rule that would require direct-to-consumer television advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product. Although some of these and other proposals will require authorization through additional legislation to become effective, members of Congress and the Trump Administration have stated that they will continue to seek new legislative and 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. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our products or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition and prospects.

More recently, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017 ("Right to Try Act") was signed into law. The law, among other things, provides a federal framework for patients to access certain investigational new drug products that have completed a Phase 1 clinical trial. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA approval under the FDA expanded access program.

In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize any of our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than European Union, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with European Union and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize any products for which we obtain marketing approval. In international markets, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we or our collaborators are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or our collaborators are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business.

***Our business operations and current and future relationships with investigators, health care professionals, consultants, third-party payors and customers will be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.***

Although we do not currently have any products on the market, if we obtain FDA approval for our product candidates, and begin commercializing those products in the United States, our operations may be directly, or indirectly through our prescribers, customers and third-party payors, subject to various U.S. federal and state healthcare laws and regulations, including, without limitation, the U.S. federal Anti-Kickback Statute, the U.S. federal civil and criminal false claims laws and Physician Payments Sunshine Act and regulations. Healthcare providers, physicians and others play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. These laws may impact, among other things our current business operations, including our clinical research activities proposed sales and marketing and education programs and constrain the business or financial arrangements and relationships with healthcare providers, physicians and other parties through which we market, sell and distribute our products for which we obtain marketing approval. In addition, we may be subject to patient data privacy and security regulation by both the U.S. federal government and the states in which we conduct our business. Finally, we may be subject to additional healthcare, statutory and regulatory requirements and enforcement by foreign regulatory authorities in jurisdictions in which we conduct our business. The U.S. laws that may affect our ability to operate include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration (including any kickback, bribe, or certain rebates), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the U.S. federal false claims and civil monetary penalties laws, including the civil False Claims Act, which, among other things, impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the U.S. federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services; similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH"), and its implementing regulations, and as amended again by the Modifications to the HIPAA Privacy, Security, Enforcement and Breach Notification Rules Under HITECH and the Genetic Information Nondiscrimination Act; Other Modifications to the HIPAA Rules, commonly referred to as the Final HIPAA Omnibus Rule, published in January 2013, which imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by covered entities subject to HIPAA, i.e. health plans, healthcare clearinghouses and certain healthcare providers, as well as their business associates that perform certain services for or on their behalf involving the use or disclosure of individually identifiable health information;
- the U.S. Federal Food, Drug and Cosmetic Act, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;
- the U.S. federal Physician Payments Sunshine Act, enacted as part of the ACA, and its implementing regulations, which require certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to CMS information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members;
- analogous state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including, but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers;
- state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources;
- state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities;
- state and local laws that require the registration of pharmaceutical sales representatives;
- state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and
- European and other foreign law equivalents of each of these laws, including reporting requirements detailing interactions with and payments to healthcare providers.

Ensuring that our internal operations and current and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from U.S. government funded healthcare programs, such as Medicare and Medicaid, or similar programs in other countries or jurisdictions, disgorgement, individual imprisonment, contractual damages, reputational harm, diminished profits, 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. Further, defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the physicians or other providers or entities with whom we expect to do business is found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment. If any of the above occur, it could adversely affect our ability to operate our business and our results of operations.

***We may not be able to obtain or maintain orphan drug designation or exclusivity for our product candidates.***

We have obtained orphan drug designation in the United States for troriluzole in SCA, BHV-0223 in ALS, BHV-5000 in Rett syndrome and verdiperstat in multiple system atrophy. We may seek orphan drug designation for other product candidates in the future. Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States.

Our ability to obtain orphan drug exclusivity for BHV-0223 for ALS is contingent upon a showing that BHV-0223 is clinically superior to Rilutek and Tiglutik in the treatment of ALS. Clinical superiority may be demonstrated by showing that a drug has greater effectiveness than the approved drug, greater safety in a substantial portion of the target population, or otherwise makes a major contribution to patient care. If we are unable to demonstrate that BHV-0223 is clinically superior to other approved riluzole products, we will not be entitled to the orphan drug exclusivity for BHV-0223 for ALS, which could adversely affect our business and our ability to market and sell BHV-0223 if it is approved for sale. Additionally, if Tiglutik, or any other approved riluzole product, receives orphan exclusivity, then BHV-0223 would need to demonstrate clinical superiority to Tiglutik or such other product in order to receive either marketing approval or orphan drug exclusivity.

Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same drug for the same indication during that time period. The applicable period is seven years in the United States and ten years in the European Union. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or the EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

We cannot assure you that any future application for orphan drug designation with respect to any other product candidate will be granted. If we are unable to obtain orphan drug designation with respect to other product candidates in the United States, we will not be eligible to obtain the period of market exclusivity that could result from orphan drug designation or be afforded the financial incentives associated with orphan drug designation. Even when we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve a later drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

***Fast track designation by the FDA may not actually lead to a faster development or regulatory review or approval process and does not assure FDA approval of our product candidate.***

In May 2017, we received fast track designation from the FDA for troriluzole for the potential treatment of SCA. Fast track designation provides opportunities for frequent interactions with FDA review staff, as well as eligibility for priority review, if relevant criteria are met, and rolling review. Fast track designation is intended to facilitate and expedite development and review of an NDA to address unmet medical needs in the treatment of serious or life-threatening conditions. However, fast track designation does not accelerate clinical trials or mean that the regulatory requirements are less stringent, nor does it ensure that troriluzole will receive marketing approval or that approval will be granted within any particular timeframe. We may also seek

fast track designation for our other product candidates. We may not experience a faster development process, review or approval compared to conventional FDA procedures. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

**Risks Related to Our Intellectual Property**

***If we are unable to obtain and maintain patent protection for product candidates, we may not be able to compete effectively in our markets.***

Market exclusivity for pharmaceutical products is based upon patent rights and certain regulatory forms of exclusivity. The failure to obtain patents of commercially relevant scope, or limitations on the use or loss of patent rights, could have a negative effect on our business. In addition, the patent environment can be unpredictable and the validity and enforceability of patents cannot be predicted with certainty. Absent relevant patent protection for a product, once the regulatory exclusivity periods expire, generic versions can be approved and marketed. Regulatory forms of exclusivity vary from country-to-country and are not available in certain countries.

We rely upon patents to protect the intellectual property related to our development programs and product candidates. Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our current and future product candidates. We have sought to protect our proprietary positions by filing and in-licensing patents and patent applications.

The patent prosecution process is expensive and time-consuming, and we or our licensors may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions. None of our patent applications claiming troriluzole or BHV-0223 have issued in major markets, but and applications filed under the Patent Cooperation Treaty, or PCT, with respect to troriluzole and BHV-0223 have been nationalized and are pending in the U.S., European countries, Japan, Korea, China, India, Russia, Brazil, Canada, and other countries. It is also possible that we will fail to identify patentable aspects of our research and development in time to obtain patent protection. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our current and future product candidates, including BHV-0223 and troriluzole, in the United States or in other foreign countries. If the patent applications we hold or have in-licensed with respect to our development programs and product candidates fail to issue, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for our current and future product candidates, it could dissuade companies from collaborating with us to develop product candidates, and threaten our ability to commercialize, products. Any such outcome could have a negative effect on our business.

The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Publications of discoveries in scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions remain confidential for a period of time after filing, and some remain so until issued. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, and such prior art could potentially invalidate one or more of our patents or prevent a patent from issuing from one or more of our pending patent applications. There is also no assurance that there is not prior art of which we are aware, but which we do not believe affects the validity, patentability or enforceability of a claim in our patents and patent applications, which may, nonetheless, ultimately be found to affect the validity, patentability or enforceability of a claim.

Even if patents are granted and even if such patents cover our current or future product candidates, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed, invalidated or held unenforceable, which could allow third parties to compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Any successful opposition to these patents or any other patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our product candidates, prevent others from designing around our claims or provide us with a competitive advantage. Any of these outcomes could impair our ability to prevent competition from third parties. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

We, independently or together with our licensors, have filed several patent applications covering various aspects of our product candidates. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such patent, or whether any issued patents will be found invalid and unenforceable or will be challenged by third parties. Any successful opposition to these patents or any other patents owned by or licensed to us after patent issuance could deprive us of rights

necessary for the successful commercialization of any product candidates that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

***Our patents and pending patent applications related to troriluzole and BHV-0223 only protect or seek to protect the formulation, prodrug or method of administration of our product candidates and not the active pharmaceutical ingredient, riluzole, a compound for which patent protection is no longer available.***

We own several families of patent applications covering prodrugs and formulations of riluzole. These patent applications include several U.S. applications and corresponding international and PCT applications. These families of patent applications cover troriluzole and numerous other prodrugs of riluzole as well as BHV-0223, a sublingual or ODT form of riluzole. Other patent applications provide coverage for alternative formulations of riluzole prodrugs and their uses. The applications also cover prodrugs related to riluzole and prodrugs relating to lanicemine. The patent for riluzole, which is the active pharmaceutical ingredient in these product candidates, expired in 2013, and so only novel riluzole-containing pharmaceutical compositions and their uses can be protected by one or more patent applications.

***We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent which might adversely affect our ability to develop and market our product candidates.***

We cannot guarantee that any of our or our licensors' patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction. Patent applications in the United States and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our product candidates could have been filed by others without our knowledge. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates or the use of our product candidates. The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our product candidates. We may incorrectly determine that our product candidates are not covered by a third-party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our product candidates.

If we fail to identify and correctly interpret relevant patents, we may be subject to infringement claims. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we fail in any such dispute, in addition to being forced to pay damages, we may be temporarily or permanently prohibited from commercializing any of our product candidates that are held to be infringing. We might, if possible, also be forced to redesign product candidates so that we no longer infringe the third- party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

***We are dependent on licensed intellectual property. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing our product candidates, if approved. If we breach any of the agreements under which we license the use, development and commercialization rights to our product candidates or technology from third parties or, in certain cases, we fail to meet certain development deadlines, we could lose license rights that are important to our business.***

We are a party to a number of license agreements under which we are granted rights to intellectual property that are important to our business and we may need or choose to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose on us, various development, regulatory and/or commercial diligence obligations, payment of milestones and/or royalties and other obligations. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license. Our business could suffer, for example, if any current or future licenses terminate, if the licensors fail to abide by the terms of the license, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms.

Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners;
- our right to transfer or assign the license; and
- the effects of termination.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

We have entered into several licenses to support our various programs. Termination of any of these license agreements would have a material adverse impact on our ability to develop and commercialize derived products under each respective agreement.

We may enter into additional licenses to third-party intellectual property that are necessary or useful to our business. Our current licenses and any future licenses that we may enter into impose various royalty payment, milestone, and other obligations on us. Under some license agreements, we may not control prosecution of the licensed intellectual property, or may not have the first right to enforce the intellectual property. In those cases, we may not be able to adequately influence patent prosecution or enforcement, or prevent inadvertent lapses of coverage due to failure to pay maintenance fees. If we fail to comply with any of our obligations under a current or future license agreement, the licensor may allege that we have breached our license agreement, and may accordingly seek to terminate our license. Termination of any of our current or future licenses could result in our loss of the right to use the licensed intellectual property, which could materially adversely affect our ability to develop and commercialize a product candidate or product, if approved, as well as harm our competitive business position and our business prospects. Under some license agreements, termination may also result in the transfer of or granting in rights under certain of our intellectual property and information related to the product candidate being developed under the license, such as regulatory information.

In addition, if our licensors fail to abide by the terms of the license, if the licensors fail to prevent infringement by third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms, our business could suffer.

***Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.***

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the statutory expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product candidate, we may be open to competition from competitive medications, including generic medications. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing product candidates similar or identical to ours.

Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments, and similar legislation in the European Union. The Hatch-Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. However, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. In the United States, only one patent per approved product can be extended, and the extension cannot extend the total patent term

beyond fourteen years from approval. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be reduced. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case. Because riluzole has already been approved, we will not be eligible to obtain patent term extension for any of our patents, should they issue, that cover BHV-0223.

***If we are unable to obtain licenses from third parties on commercially reasonable terms or fail to comply with our obligations under such agreements, our business could be harmed.***

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. If we are unable to license such technology, or if we are forced to license such technology, on unfavorable terms, our business could be materially harmed. If we are unable to obtain a necessary license, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us.

If we fail to comply with our obligations under license agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market, or may be forced to cease developing, manufacturing or marketing, any product that is covered by these agreements or may face other penalties under such agreements. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, cause us to lose our rights under these agreements, including our rights to important intellectual property or technology or impede, delay or prohibit the further development or commercialization of one or more product candidates that rely on such agreements.

***Intellectual property rights do not necessarily address all potential threats to our business.***

Once granted, patents may remain open to invalidity challenges including opposition, interference, re-examination, post-grant review, inter partes review, nullification or derivation action in court or before patent offices or similar proceedings for a given period after allowance or grant, during which time third parties can raise objections against such grant. In the course of such proceedings, which may continue for a protracted period of time, the patent owner may be compelled to limit the scope of the allowed or granted claims which are the subject of the challenge, or may lose the allowed or granted claims altogether.

In addition, the degree of future protection afforded by our intellectual property rights is uncertain because even granted intellectual property rights have limitations, and may not adequately protect our business or our innovations or permit us to maintain our competitive advantage. Moreover, if a third party has intellectual property rights that cover the practice of our technology, we may not be able to fully exercise or extract value from our intellectual property rights. The following examples are illustrative:

- others may be able to develop and/or practice technology that is similar to our technology or aspects of our technology, such as compounds or formulations that are similar to our product candidates, but that are not covered by the claims of the patents that we own or control, assuming such patents have issued or do issue;
- we or our licensors or any future strategic partners might not have been the first to conceive or reduce to practice the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed;
- we or our licensors or any future 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 advantage, 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;

- third parties performing manufacturing or testing for us using our product candidates or technologies could use the intellectual property of others without obtaining a proper license;
- parties may assert an ownership interest in our intellectual property and, if successful, such disputes may preclude us from exercising exclusive rights over that intellectual property;
- we may not develop or in-license additional proprietary technologies that are patentable;
- we may not be able to obtain and maintain necessary licenses on commercially reasonable terms, or at all; and
- the patents of others may have an adverse effect on our business.

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

***Changes in intellectual property laws or jurisprudence could impair our ability to protect our product candidates.***

Changes in intellectual property laws or regulations in the U.S., or other countries, could negatively affect our business. Similarly, changes in the interpretation of such laws or regulations could have an impact on our business.

The current law in the United States, as in most other countries in the world, uses a "first-to-file" system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. This requires that we promptly file patent applications on our inventions. The failure to do so could result in another patent applicant being awarded a patent, even though we may have made the invention first. Current U.S. law also provides a lower evidentiary standard in U.S. Patent and Trademark Office ("USPTO") proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim. Hence, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action.

Additionally, the U.S. Supreme Court has ruled on several patent cases in recent years, such as Impression Products, Inc. v. Lexmark International, Inc., Association for Molecular Pathology v. Myriad Genetics, Inc. (Myriad I), Mayo Collaborative Services v. Prometheus Laboratories, Inc., and Alice Corporation Pty. Ltd. v. CLS Bank International, 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 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 U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

***Some intellectual property which we have in-licensed may have been discovered through government funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements, and a preference for U.S. industry. Compliance with such regulations may limit our exclusive rights, and limit our ability to contract with non-U.S. manufacturers.***

Some of the intellectual property rights we have licensed or acquired, including rights licensed to us by Rutgers, the State University of New Jersey, and rights assigned to us by ALS Biopharma may have been generated through the use of U.S. government funding and may therefore be subject to certain federal regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh-Dole Act of 1980 ("Bayh-Dole Act"). These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). The U.S. government also has the right to take title to these inventions if we, or the applicable licensor, fail to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us or the applicable licensor to expend substantial resources. In addition, the U.S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. To the extent any of our current or future intellectual property is generated through the use of U.S.

government funding, the provisions of the Bayh-Dole Act may similarly apply. Any exercise by the government of certain of its rights could harm our competitive position, business, financial condition, results of operations and prospects.

***Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a negative impact on the success of our business.***

Generic manufacturers as well as other groups seeking financial gain are also increasingly seeking to challenge patents before they expire. Our commercial success depends, in part, upon our ability, and the ability of our future collaborators, to develop, manufacture, market and sell our product candidates, if approved, and use our proprietary technologies without alleged or actual infringement, misappropriation or other violation of the patents and proprietary rights of third parties. There have been many lawsuits and other proceedings involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, inter partes reviews, post grant reviews and re-examination proceedings before the USPTO, and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates. Some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the intellectual property rights of third parties.

We may in the future become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates and technology, including interference or derivation proceedings, post grant review and inter partes review before the USPTO or similar adversarial proceedings or litigation in other jurisdictions. Similarly, we or our licensors or collaborators may initiate such proceedings or litigation against third parties, including to challenge the validity or scope of intellectual property rights controlled by third parties. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, and the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire or are finally determined to be invalid or unenforceable. Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our technology, such as our compositions, formulations, or methods of treatment, prevention or use, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires or is finally determined to be invalid, unenforceable or not infringed by our technology. In either case, such a license may not be available on commercially reasonable terms, or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. Furthermore, even in the absence of litigation, we may need or may choose to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In such an event, we would be unable to further practice our technologies or develop and commercialize any of our product candidates at issue, which could harm our business significantly.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates, if approved. If, in the context of seeking approval for one of our product candidates subject to approval via Section 505(b)(2), we were required to file a Paragraph IV certification against any patents of a third party, we would additionally be at risk of an automatic stay if litigation is initiated, thereby potentially delaying our approval or market entry. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. Third parties making such claims may have the ability to dedicate substantially greater resources to these legal actions than we or our licensors or collaborators can. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

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

Competitors may infringe or otherwise violate our or our licensors' patents or misappropriate or otherwise violate our or our licensor's other intellectual property rights. To counter infringement or unauthorized use, we may be required to file legal claims, which can be expensive and time-consuming. Our adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any

litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

The initiation of a claim against a third party may also cause the third party to bring counter claims against us such as claims asserting that our patents are invalid or unenforceable or claims challenging the scope of the intellectual property rights we own or control. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement, lack of adequate written description or lack of statutory subject matter. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant material information from the USPTO, or made a materially misleading statement, during prosecution. Third parties may also raise similar validity claims before the USPTO in post-grant proceedings such as ex parte re-examinations, inter partes review, or post-grant review, or oppositions or similar proceedings outside the United States, in parallel with litigation or even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. We cannot be certain that there is no invalidating prior art, of which we, our licensors and the patent examiner were unaware during prosecution.

For the patents and patent applications that we have licensed, we may have limited or no right to participate in the defense of any licensed patents against challenge by a third party. Therefore, these patents and applications may not be defended in a manner consistent with the best interests of our business. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of any future patent protection on our current or future product candidates. Such a loss of patent protection could harm our business. In addition, if the breadth or strength of protection provided by our or our licensors' patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

We may not be able to prevent, alone or with our licensors, infringement or misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Any litigation or other proceedings to enforce our intellectual property rights may fail, and even if successful, may result in substantial costs and distract our management and other employees.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have an adverse effect on the price of our common shares.

***We may not be able to protect our intellectual property rights throughout the world, which could negatively impact our business.***

Filing, prosecuting and defending patents covering our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Further, licensing partners may not prosecute patents in certain jurisdictions in which we may obtain commercial rights, thereby precluding the possibility of later obtaining patent protection in these countries. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export 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 product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from 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, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents, if obtained, or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights, whether owned or licensed to us, in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions

in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets.

Additionally, the requirements for patentability may differ in certain countries, particularly developing countries. For example, unlike other countries, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed drug. In India, unlike the United States, there is no link between regulatory approval of a drug and its patent status. Furthermore, generic drug manufacturers or other competitors may challenge the scope, validity or enforceability of our or our licensors' patents, requiring us or our licensors to engage in complex, lengthy and costly litigation or other proceedings. Generic drug manufacturers may develop, seek approval for, and launch generic versions of our products. In addition to India, certain countries in Europe and developing countries, including China, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we and our licensors may have limited remedies if patents are infringed or if we or our licensors are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our and our licensors' efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license.

***We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of their former employers or other third parties.***

We do and may employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our licensors, competitors or potential competitors. Although we try to ensure that our employees, consultants and independent contractors do not use the proprietary information or know-how of others in their work for us, and we are not currently subject to any claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties, we may in the future be subject to such claims. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

***We may be subject to claims challenging the inventorship or ownership of our patents, patent applications or other intellectual property, or our licensors may be subject to similar such claims.***

Although we are not currently experiencing any claims challenging the inventorship or ownership of our patents or ownership of our intellectual property, we may in the future be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co-inventor, or that an employee, consultant, or other third party performed work for us that conflicts with that person's obligations to a third party, such as an employer, and thus, that the third party has an ownership interest in the intellectual property arising out of work performed for us. While it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. For example, the assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, or we may have disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. This risk similarly applies to any intellectual property that we in-license. If a licensor is subject to a claim challenging inventorship or ownership, it could adversely impact our exclusivity under or rights to use valuable in-licensed intellectual property.

***Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.***

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time-consuming and is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common shares.

Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities.

We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon, misappropriating or successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have an adverse effect on our ability to compete in the marketplace.

***Our inability to protect our confidential information and trade secrets would harm our business and competitive position.***

In addition to seeking patents for some of our technology and product candidates, via intellectual property we own or license, 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 confidentiality and invention or patent assignment agreements with our employees and consultants. We also seek to preserve the integrity and confidentiality of our data, trade secrets and know-how by maintaining physical security of our premises and physical and electronic security of our information technology systems. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. We cannot guarantee that our trade secrets and other proprietary and confidential information will not be disclosed or that competitors will not otherwise gain access to our trade secrets. 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 both within and outside the United States may be less willing or unwilling to protect trade secrets. Moreover, if a competitor lawfully obtained or independently developed any of our trade secrets, we would have no right to prevent such competitor from using that technology or information to compete with us. Any misappropriation, disclosure or independent development of our trade secrets could harm our competitive position.

Trade secrets and know-how can be difficult to protect as trade secrets and know-how will over time be disseminated within the industry through independent development, the publication of journal articles, and the movement of personnel skilled in the art from company to company or academic to industry scientific positions. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. If we are unable to prevent material disclosure of the intellectual property related to our technologies to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could adversely affect our business, results of operations and financial condition. Even if we are able to adequately protect our trade secrets and proprietary information, our trade secrets could otherwise become known or could be independently discovered by our competitors. Competitors could purchase our products and attempt to replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe our intellectual property rights, design around our protected technology or develop their own competitive technologies that fall outside of our intellectual property rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, in the absence of patent protection, we would have no right to prevent them, or those to whom they communicate, from using that technology or information to compete with us.

We may not be able to prevent misappropriation of our intellectual property, trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common shares.

***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.***

Periodic maintenance and annuity fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could

result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain the patents and patent applications covering our products, our competitors might be able to enter the market, which would harm our business. In addition, to the extent that we have responsibility for taking any action related to the prosecution or maintenance of patents or patent application in-licensed from a third party, any failure on our part to maintain the in-licensed rights could jeopardize our rights under the relevant license and may expose us to liability.

**Risks Related to Our Business Operations, Employee Matters and Managing Growth**

***Our future growth and ability to compete depends on retaining our key personnel and recruiting additional qualified personnel.***

We are highly dependent on the management, development, clinical, financial and business development experience of our senior management. Although we have entered into employment agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or employees.

The competition for qualified personnel in the biopharmaceutical field is intense, and our future success depends upon our ability to attract, retain and motivate highly-skilled scientific, technical and managerial employees. We face competition for personnel from other companies, universities, public and private research institutions and other organizations. If our recruitment and retention efforts are unsuccessful in the future, it may be difficult for us to implement business strategy, which could harm our business.

In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

***Our future growth depends, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.***

Our future profitability will depend, in part, on our ability to commercialize our product candidates in markets outside of the United States and the European Union. If we commercialize our product candidates in foreign markets, we will be subject to additional risks and uncertainties, including:

- economic weakness, including inflation, or political instability in particular economies and markets;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements, many of which vary between countries;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- tariffs and trade barriers;
- other trade protection measures, import or export licensing requirements or other restrictive actions by U.S. or foreign governments;
- longer accounts receivable collection times;
- longer lead times for shipping;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad ;
- workforce uncertainty in countries where labor unrest is common;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries, and related prevalence of generic alternatives to therapeutics;
- foreign currency exchange rate fluctuations and currency controls;
- differing foreign reimbursement landscapes;
- uncertain and potentially inadequate reimbursement of our products; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Foreign sales of our products could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs.

***Laws and regulations governing our international operations may preclude us from developing, manufacturing and selling certain product candidates and products outside of the United States and require us to develop and implement costly compliance programs.***

As we expand our operations outside of the United States, we will be required to dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate, as well as with the Foreign Corrupt Practices Act ("FCPA"), compliance with which is expensive and difficult, particularly in countries in which corruption is a recognized problem. As a result, these laws may preclude us from developing, manufacturing or selling certain product candidates outside of the United States, which could limit our growth potential and increase our development costs. The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

***We expect to expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.***

As of December 31, 2018, we had 63 employees, all of which were employed directly by our U.S. subsidiary, Biohaven Pharmaceuticals, Inc. As our clinical development progresses, we expect to experience growth in the number of our employees and the scope of our operations, particularly in the areas of clinical operations, regulatory affairs and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

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

We are exposed to the risk that our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless or negligent conduct or unauthorized activities that violates (1) the laws and regulations of the FDA, the EMA and other similar regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities, (2) manufacturing standards, (3) federal and state data privacy, security, fraud and abuse and other healthcare laws and regulations in the United States and abroad and (4) laws that require the true, complete and accurate reporting of financial information or data. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct by these parties could also involve the improper use of individually identifiable information, including information obtained in the course of clinical trials, creating fraudulent data in our preclinical studies or clinical trials or illegal misappropriation of product candidates, which could result in regulatory sanctions and serious harm to our reputation.

Although we have adopted a code of business conduct and ethics, it is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity 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. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, including damages, fines, disgorgement, imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, 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 and the curtailment or restructuring of our operations.

***We may be subject to securities litigation, which is expensive and could divert management attention.***

Our share price has been, and may continue to be, volatile, and in the past companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. This risk is especially relevant for us because biotechnology companies have experienced significant stock price volatility in recent years. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

***Our business and operations may be materially adversely affected in the event of computer system failures or security breaches.***

Despite the implementation of security measures, our internal computer systems, and those of our CROs and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, cyberattacks, natural disasters, fire, terrorism, war and telecommunication and electrical failures. If such an event were to occur and interrupt our operations, it could result in a material disruption of our development programs. For example, the loss of clinical trial data from 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, loss of trade secrets or inappropriate disclosure of confidential or proprietary information, including protected health information or personal data of employees or former employees, access to our clinical data or disruption of the manufacturing process, we could incur liability and the further development of our product candidates could be delayed. We may also be vulnerable to cyberattacks by hackers or other malfeasance. This type of breach of our cybersecurity may compromise our confidential information or our financial information and adversely affect our business or result in legal proceedings.

Additionally, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR is wide–ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third–party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time–intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with any European activities.

**Risks Related to Ownership of Our Common Shares**

***An active trading market for our common shares may not continue to develop or be sustained, or be liquid enough for investors to resell our common shares quickly or at the market price.***

Prior to May 4, 2017, there was no public market for our common shares, and we cannot assure you that an active trading market will continue to develop or be sustained. If an active market for our common shares does not develop or is not sustained, it may be difficult for our shareholders to sell shares without depressing the market price for the shares or to sell their shares at all.

***The trading price of our common shares has been, and may continue to be, volatile and may fluctuate due to factors beyond our control, and purchasers of our common shares could incur substantial losses.***

Our share price has been and may continue to be volatile. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their common shares at or above the price paid for the shares. The market price for our common shares may be influenced by many factors, including:

- positive or negative results, including preliminary or topline results, of preclinical studies and clinical trials reported by us, strategic partners or competitors;
- any delay in the commencement, enrollment and the ultimate completion of clinical trials;
- technological innovations or commercial product introductions by us or competitors;
- failure to successfully develop and commercialize any of our product candidates;

- developments, announcements or changes in government regulations relating to drug products, including related to drug pricing, reimbursement and healthcare coverage;
- delays in in-licensing or acquiring additional complementary product candidates;
- developments concerning proprietary rights, including patents and litigation matters;
- public concern relating to the commercial value or safety of any of our product candidates;
- financing or other corporate transactions, or inability to obtain additional funding;
- announcements relating to our arrangements with BMS, AstraZeneca or RPI;
- failure to meet or exceed expectations of the investment community;
- actual or anticipated variations in our operating results;
- changes in financial estimates by us or by any securities analysts who might cover our shares;
- announcements by therapeutic drug product providers related to pricing of therapeutics;
- announcements of significant licenses, acquisitions, strategic partnerships or joint ventures by us or our competitors;
- publication of research reports or comments by securities or industry analysts;
- recruitment or departure of key personnel;
- sales of our common shares, including sales by our directors and officers or specific shareholders;
- general market or regulatory conditions in the pharmaceutical industry or in the economy as a whole; or
- other events and factors, many of which are beyond our control.

These and other market and industry factors may cause the market price and demand for our securities to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from selling their common shares at or above the price paid for the shares and may otherwise negatively affect the liquidity of our common shares.

Some companies that have experienced volatility in the trading price of their shares have been the subject of securities class action litigation. Any lawsuit to which we are a party, with or without merit, may result in an unfavorable judgment. We also may decide to settle lawsuits on unfavorable terms. Any such negative outcome could result in payments of substantial damages or fines, damage to our reputation or adverse changes to our offerings or business practices. Defending against litigation is costly and time-consuming, and could divert our management's attention and resources. Furthermore, during the course of litigation, there could be negative public announcements of the results of hearings, motions or other interim proceedings or developments, which could have a negative effect on the market price of our common shares.

***If securities or industry analysts do not publish research, or publish inaccurate or unfavorable research, about our business, the price of our common shares and our trading volume could decline.***

The trading market for our common shares will depend in part on the research and reports that securities or industry analysts publish about us or our business. As a newly public company, we have only limited research coverage by equity research analysts. Equity research analysts may elect not to initiate or to continue to provide research coverage of our common shares, and such lack of research coverage may adversely affect the market price of our common shares. Even if we do have equity research analyst coverage, we will not have any control over the analysts or the content and opinions included in their reports. The price of our shares could decline if one or more equity research analysts downgrade our shares or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our shares could decrease, which in turn could cause our share price or trading volume to decline.

***Concentration of ownership of our common shares among our executive officers, directors and their affiliated entities may prevent new investors from influencing significant corporate decisions.***

Our directors and executive officers, and entities affiliated with them, in the aggregate, beneficially own approximately 24% of our common shares. These shareholders, acting together, would be able to control or significantly influence all matters requiring shareholder approval, including the election and removal of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. Some of these persons or entities may have interests different than yours. For example, because many of these shareholders purchased their shares at prices substantially below the current market price of our common shares and have held their shares for a longer period, they may be more interested in selling our company to an acquirer than other investors, or they may want us to pursue strategies that deviate from the interests of other shareholders.

***Provisions in our memorandum and articles of association could make an acquisition of us, which may be beneficial to our shareholders, more difficult and may prevent attempts by our shareholders to replace or remove our current management and limit the market price of our common shares.***

Provisions in our memorandum and articles of may discourage, delay or prevent a merger, acquisition or other change in control of us that shareholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions also could limit the price that investors might be willing to pay in the future for our common shares, thereby depressing the market price of our common shares. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our shareholders to replace or remove our current management by making it more difficult for shareholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which shareholders can remove directors from the board;
- establish advance notice requirements for shareholder proposals that can be acted on at shareholder meetings and nominations to our board of directors;
- require that shareholder actions must be effected at a duly called shareholder meeting and prohibit actions by our shareholders by written consent;
- limit who may call shareholder meetings;
- authorize our board of directors to issue preferred shares without shareholder approval, which could be used to institute a shareholder rights plan, or so-called "poison pill," that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our shareholders would be entitled to cast to amend or repeal certain provisions of our memorandum and articles of association.

Any provision of our memorandum and articles of association or BVI law that has the effect of delaying or deterring a change of control could limit the opportunity for our shareholders to receive a premium for their common shares, and could also affect the price that some investors are willing to pay for our common shares.

***Sales of a substantial number of our common shares in the public market could occur at any time. This could cause the market price of our common shares to drop significantly, even if our business is doing well.***

Sales of a substantial number of our common shares in the public market, or the perception that these sales might occur, could depress the market price of our common shares and could impair our ability to raise capital through the sale of additional equity securities.

As of February 26, 2019, we had 44,262,658 common shares outstanding, and 44,262,658 of these shares are freely tradable without restrictions or further registration under the Securities Act except, subject to certain restrictions applicable to shares held by our affiliates as defined in Rule 144 under the Securities Act.

In addition, we have filed a registration statement on Form S-8 registering the issuance of 12,849,968 common shares subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. Shares registered under this registration statement on Form S-8 are available for sale in the public market subject to vesting arrangements and exercise of options for granted awards and, in the case of our affiliates, the restrictions of Rule 144.

Additionally, the holders of approximately 7.9 million common shares, or their transferees, have rights, subject to some conditions, to require us to file one or more registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other shareholders. If we were to register the resale of these shares, they could be freely sold in the public market without limitation. If these additional shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common shares could decline.

***Because we do not expect to pay dividends on our common shares in the foreseeable future, capital appreciation, if any, would be your sole source of gain.***

We have never declared or paid any dividends on our common shares. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. The decision to pay future dividends to shareholders will be at the discretion of our board of directors after taking into account various factors including our business prospects, cash requirements, financial performance

and new product development. Accordingly, investors cannot rely on dividend income from our common shares and any returns on an investment in our common shares will likely depend entirely upon any future appreciation in the price of our common shares.

***We will have broad discretion in the use of our existing cash, and may invest or spend our cash in ways with which you do not agree and in ways that may not increase the value of your investment.***

We will have broad discretion over the use of our cash. You may not agree with our decisions, and our use of cash may not yield any return on your investment. We expect to use our existing cash to advance and expand the development of our CGRP receptor antagonist platform, including our planned NDA filings in 2019, and glutamate modulation platform product candidates, begin development of our myeloperoxidase platform and for working capital and general corporate purposes, including satisfaction of any of our milestone payment obligations under our license agreements. In addition, we may use a portion of our existing cash to pursue our strategy to in-license or acquire additional drug candidates. Our failure to apply our cash effectively could compromise our ability to pursue our growth strategy and we might not be able to yield a significant return, if any, on our investment of this cash. You will not have the opportunity to influence our decisions on how to use our cash.

***We will continue to incur increased costs as a result of operating as a public company, and our management and board of directors will be required to devote substantial time to new compliance initiatives and corporate governance practices.***

As a public company listed in the United States, we have and will continue to, incur significant incremental legal, accounting and other expenses. These costs could negatively affect our financial results. In addition, changing laws, regulations and standards relating to corporate governance and public disclosure, including regulations implemented by the SEC and the New York Stock Exchange, may increase legal and financial compliance costs and make some activities more time consuming. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue-generating activities to compliance activities.

Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may 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, which in turn could make it more difficult for us to attract and retain qualified members of our management and board of directors.

In addition, these rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. If, notwithstanding our efforts to comply with new laws, regulations and standards, we fail to comply, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

Our management is also required to annually evaluate our internal control over financial reporting and include a report on the effectiveness of these controls in our Annual Reports on Form 10-K. If we are unable to continue to conclude that we have effective internal control over financial reporting or, if our independent registered public accounting firm is unable to provide us with an unqualified report as to the effectiveness of our internal controls over financial reporting, investors could lose confidence in the reliability of our financial statements, which could result in a decrease in the value of our common stock.

***The holders of our common shares may have fewer protections as a shareholder of our company, as the rights of shareholders under BVI law differ from those under U.S. law.***

Our corporate affairs are governed by our memorandum and articles of association, the BVI Business Companies Act, 2004 (the "BVI Act") and the common law of the BVI. The rights of shareholders to take legal action against our directors, actions by minority shareholders and the fiduciary responsibilities of our directors under BVI law are to a large extent governed by the common law of the BVI and by the BVI Act. The common law of the BVI is derived in part from comparatively limited judicial precedent in the BVI as well as from English common law, which has persuasive, but not binding, authority on a court in the BVI. The rights of our shareholders and the fiduciary responsibilities of our directors under BVI law therefore are not as clearly established as they would be under statutes or judicial precedents in some jurisdictions in the United States. In particular, the BVI has a less developed body of securities laws as compared to the United States, and some states, such as Delaware, have more fully developed and judicially interpreted bodies of corporate law.

As a result of all of the above, holders of our common shares may have more difficulty in protecting their interests through actions against our management, directors or major shareholders than they would as shareholders of a U.S. company. They may have greater difficulty securing legal advice about the law of the BVI than they would U.S. and state law, and the relatively less developed nature of that country's securities law may leave investors with less certainty about the validity and strength of any

claims they believe they may have against us. In addition, other differences between BVI and U.S. law, as well as the terms of our articles of association, may result in shareholders having different potential influence than they would under various U.S. state laws with respect to matters such as officer and director actions, mergers and acquisitions, takeover efforts, and other corporate decision making.

***Shareholders in BVI business companies may not be able to initiate shareholder derivative actions, thereby depriving a shareholder of the ability to protect its interests.***

While statutory provisions do exist in BVI law for derivative actions to be brought in certain circumstances, shareholders in BVI business companies may not have standing to initiate a shareholder derivative action in a federal court of the United States. The circumstances in which any such action may be brought, and the procedures and defenses that may be available in respect to any such action, may result in the rights of shareholders of a BVI business company being more limited than those of shareholders of a company organized in the United States. Accordingly, shareholders may have fewer alternatives available to them if they believe that corporate wrongdoing has occurred. The BVI courts are also unlikely to: (i) recognize or enforce against us judgments of courts in the United States based on certain civil liability provisions of U.S. securities law; or (ii) to impose liabilities against us, in original actions brought in the BVI, based on certain civil liability provisions of U.S. securities laws that are penal in nature or that relate to taxes or similar fiscal or revenue obligations or would be viewed as contrary to BVI public policy or the proceedings pursuant to which judgment was obtained were contrary to natural justice. There is no statutory recognition in the BVI of judgments obtained in the United States, although any final and conclusive monetary judgment obtained against a BVI business company in a U.S. court, for a definite sum, may be treated by the courts of the BVI as a cause of action in itself so that no retrial of the issues would be necessary provided that in respect of the judgment of the U.S. court:

- The U.S. court issuing the judgment had jurisdiction in the matter and the company either submitted to such jurisdiction or was resident or carrying on business within such jurisdiction and was duly served with process;
- The judgment given by the U.S. court was not in respect of penalties, taxes, fines or similar fiscal or revenue obligations of the company;
- In obtaining judgment there was no fraud on the part of the person in whose favor judgment was given or on the part of the U.S. court;
- Recognition or enforcement of the judgment in the BVI would not be contrary to public policy; and
- The proceedings pursuant to which judgment was obtained were not contrary to natural justice.

***The laws of the BVI relating to the protection of minority shareholders differ from those under U.S. law and, in some circumstances, may offer less protection.***

The BVI Act includes the following statutory remedies which minority shareholders in the company can rely upon:

- If the company or a director of the company engages in or proposes to engage in conduct, that contravenes the BVI Act or our memorandum and articles of association, a shareholder may apply to the BVI court for an order directing the company or its director(s) to comply with or restraining the company or a director from engaging in conduct that contravenes the BVI Act or our memorandum and articles of association.
- Under the BVI Act, minority shareholders have a statutory right to bring a derivative action in the name of and on behalf of the company in circumstances where the company has cause of action against its directors. This remedy is available at the discretion of the BVI court which will take a number of factors into account before granting or refusing a leave to proceed to the relevant shareholder, including whether such action is in the interests of the company, the cost of such action and whether there are alternative remedies that the shareholder concerned may rely upon.
- A shareholder of the company may bring an action against the company for breach of duty owed to him or her as a shareholder. This would typically be relevant in a situation where a shareholder is aggrieved by the company for breach of an entitlement or right under the company's memorandum and articles of association.
- A shareholder of the company who considers that the affairs of the company have been, are being or likely to be, conducted in a manner that is, or any act or acts of the company have been, or are, likely to be oppressive, unfairly discriminatory, or unfairly prejudicial to him in that capacity, may apply to the BVI court for an order to remedy the situation. Again, this is a discretionary remedy and the BVI court will only award it if they are satisfied that it is just and equitable to do so.

- A shareholder may apply for a liquidation of the company under the Insolvency Act 2003 of the BVI, and the BVI court should not refuse such an application merely because there are no assets to distribute to the shareholder. Shareholders can also by resolution appoint a liquidator of a BVI business company under the BVI Act if the company is solvent or under the Insolvency Act 2003 if the company is insolvent.

In addition to the statutory rights outlined above, there are common law rights for the protection of shareholders that may be invoked, largely dependent on English common law. Under the general rule pursuant to English common law known as the rule in Foss v. Harbottle, a court will generally refuse to interfere with the management of a company at the insistence of a minority of its shareholders who express dissatisfaction with the conduct of the company's affairs by the majority or the board of directors. However, every shareholder is entitled to have the affairs of the company conducted properly according to law and the constituent documents of the company. As such, if those who control the company have persistently disregarded the requirements of company law or the provisions of the company's memorandum and articles of association, then the courts will grant relief. Generally, the areas in which the courts will intervene are the following: (1) an act complained of which is outside the scope of the authorized business or is illegal or not capable of ratification by the majority; (2) acts that constitute fraud on the minority where the wrongdoers control the company; (3) acts that infringe on the personal rights of the shareholders, such as the right to vote; and (4) where the company has not complied with provisions requiring approval of the shareholders, which are more limited than the rights afforded minority shareholders under the laws of many states in the United States.

Having regard to the above, the protection available to minority shareholders under BVI law may be more limited than under the laws of some jurisdictions in the United States.

***Risks related to recent and potential changes to regulatory legislation in the British Virgin Islands could lead to increased costs for us to comply with additional regulatory and reporting requirements.***

As the global regulatory and tax environment evolves, we may be subject to new or different statutory and regulatory requirements. For example, on January 1, 2019 the Economic Substance (Companies and Limited Partnerships) Act, 2018 of the British Virgin Islands (the "Economic Substance Act") came into force and related regulations and guidance are anticipated in due course. It is difficult to predict what impact the adoption of these laws or regulations, or changes in the interpretation of existing laws or regulations could have on us, however, compliance with various additional obligations may create additional costs that may be borne by us or otherwise affect our management and operation.

***It may be difficult to enforce a U.S. or foreign judgment against us, our directors and our officers outside the United States, or to assert U.S. securities laws claims outside of the United States.***

As a BVI business company, it may be difficult for a shareholder to effect service of process within the United States upon us, our directors and officers, or to enforce against us, or them, judgments obtained in U.S. courts, including judgments predicated upon the civil liability provisions of the securities laws of the United States or any state therein. Additionally, it may be difficult to assert U.S. securities law claims in actions originally instituted outside of the United States. Foreign courts may refuse to hear a U.S. securities law claim because foreign courts may not be the most appropriate forums in which to bring such a claim. Even if a foreign court agrees to hear a claim, it may determine that the law of the jurisdiction in which the foreign court resides, and not U.S. law, is applicable to the claim. Further, if U.S. law is found to be applicable, the content of applicable U.S. law must be proved as a fact, which can be a time-consuming and costly process, and certain matters of procedure would still be governed by the law of the jurisdiction in which the foreign court resides.

***Changes in tax law, determinations by tax authorities or changes in our effective tax rates may adversely affect our business and financial results.***

Under current law, we expect to be treated as a non-U.S. corporation for U.S. federal income tax purposes. The tax laws applicable to our business activities, however, are subject to change and uncertain interpretation. Our tax position could be adversely impacted by changes in tax rates, tax laws, tax practice, tax treaties or tax regulations or changes in the interpretation thereof by the tax authorities in jurisdictions in which we do business. Our actual tax rate may vary from our expectation and that variance may be material. A number of factors may increase our future effective tax rates, including: (1) the jurisdictions in which profits are determined to be earned and taxed; (2) the resolution of issues arising from any future tax audits with various tax authorities; (3) changes in the valuation of our deferred tax assets and liabilities; (4) our ability to use net operating loss carryforwards to offset future taxable income and any adjustments to the amount of the net operating loss carryforwards we can utilize; and (5) changes in tax laws or the interpretation of such tax laws, and changes in generally accepted accounting principles.

As a company organized under the laws of the BVI, we are principally subject to taxation in the BVI. Under the current laws of the BVI, tax on a company's income is assessed at a zero percent tax rate. For U.S. federal tax purposes, a corporation is generally considered a "domestic corporation" if it is incorporated or organized in the United States, and a "foreign corporation" if it is incorporated or organized in a non-U.S. jurisdiction. Because we are a BVI incorporated entity, we would be classified as a foreign corporation under these general rules. Section 7874 of the Code ("Section 7874") however, contains rules that can result in a foreign corporation being treated as a domestic corporation for U.S. federal tax purposes. Under Section 7874, a foreign corporation will nevertheless be treated as a domestic corporation for U.S. federal tax purposes if

(1) the foreign corporation directly or indirectly acquires substantially all of the assets held directly or indirectly by a domestic corporation (including the indirect acquisition of assets by acquisition of all the outstanding shares of a domestic corporation), (2) the shareholders of the acquired domestic corporation hold at least 80% (by either vote or value) of the shares of the acquiring foreign corporation after the acquisition by reason of holding shares in the acquired domestic corporation (including the receipt of the foreign corporation's shares in exchange for the domestic corporation's shares) (the "ownership test"), and (3) the foreign corporation's "expanded affiliated group" does not have substantial business activities in the foreign corporation's country of organization or incorporation relative to the expanded affiliated group's worldwide activities. For purposes of Section 7874, "expanded affiliated group" means the foreign corporation and all subsidiaries in which the foreign corporation, directly or indirectly, owns more than 50% of the shares by vote and value.

On December 31, 2016, we entered into an agreement with the stockholders of BPI to purchase all of the outstanding capital stock of BPI for an aggregate purchase price of $0.6 million, payable by the issuance of promissory notes to each BPI stockholder. Although we and BPI had certain shareholders in common before December 31, 2016, based on the rules for determining share ownership under Section 7874, we believe the stockholders of BPI owned less than 80% of our company. Accordingly, we do not believe that this transaction meets the ownership test under Section 7874 and therefore do not believe that we should be treated as a domestic corporation for U.S. federal tax purposes. However, the tax law in this area could be changed, including changed on a retroactive basis, and the application of Section 7874 to our acquisition of BPI could substantially increase our effective tax rate.

On December 22, 2017, President Trump signed into law new legislation, commonly known as the Tax Cuts and Jobs Act of 2017, or Tax Act, that significantly revises the Internal Revenue Code of 1986, as amended. The Tax Act, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% 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 Tax Act is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain if and to what extent various states will conform to the Tax Act. The impact of the Tax Act on holders of our common shares is also uncertain and could be adverse. We urge our shareholders to consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common shares.

We may also become subject to income, withholding or other taxes in jurisdictions by reason of our activities and operations, and it is possible that taxing authorities in such jurisdictions could assert that we are subject to greater taxation than we currently anticipate. For example, we expect to form an Irish subsidiary that will be the principal operating company for conducting our business and the entity that will hold our intellectual property rights in certain of our product candidates. This new Irish subsidiary would be subject to taxation in Ireland. In addition to the establishment of this Irish entity as our principal operating company, we, as the parent company, may also be subject to taxation in Ireland in the future, even as we remain a company organized under the laws of the BVI. Any of these transactions may result in higher tax liabilities and a higher overall effective tax rate. Any significant increase in our future effective tax rates could reduce net income for future periods.

***If we are a passive foreign investment company there could be adverse U.S. federal income tax consequences to U.S. holders.***

Under the Code, we will be a passive foreign investment company ("PFIC") for any taxable year in which (1) 75% or more of our gross income consists of passive income or (2) 50% or more of the average quarterly value of our assets consists of assets that produce, or are held for the production of, passive income. For purposes of these tests, passive income includes dividends, interest, gains from the sale or exchange of investment property and certain rents and royalties. In addition, for purposes of the above calculations, a non-U.S. corporation that directly or indirectly owns at least 25% by value of the shares of another corporation is treated as if it held its proportionate share of the assets and received directly its proportionate share of the income of such other corporation. If we are a PFIC for any taxable year during which a U.S. holder holds our shares, the U.S. holder may be subject to adverse tax consequences regardless of whether we continue to qualify as a PFIC, including ineligibility for any preferred tax rates on capital gains or on actual or deemed dividends, interest charges on certain taxes treated as deferred, and additional reporting requirements.

Although we do not believe we were a PFIC for our taxable year ended December 31, 2017 and do not currently expect to be a PFIC for our taxable year ending December 31, 2018 or future taxable years, we cannot provide any assurances regarding our PFIC status for any past, current or future taxable years. The determination of whether we are a PFIC is a fact-intensive determination made on an annual basis applying principles and methodologies which in some circumstances are unclear and subject to varying interpretation. In particular, the characterization of our assets as active or passive may depend in part on our current and intended future business plans which are subject to change. In addition, for our current and future taxable years, the

total value of our assets for PFIC testing purposes may be determined in part by reference to the market price of our shares from time to time, which may fluctuate considerably. Under the income test, our status as a PFIC depends on the composition of our income which, in our current and future taxable years, we may not be able to fully control, for example, with respect to income attributed to us from entities owned 25% or more by us. The composition of our income and assets is also affected by how, and how quickly, we spend the cash we raise in any offering, including in our recent IPO.

In certain circumstances, a U.S. holder of shares in a PFIC may alleviate some of the adverse tax consequences described above by making a "qualified electing fund" ("QEF") election to include in income its pro rata share of the corporation's income on a current basis. However, a U.S. holder may make a qualified electing fund election with respect to our common shares only if we agree to furnish such U.S. holder annually with a PFIC annual information statement as specified in the applicable U.S. Treasury Regulations. We currently do not intend to prepare or provide the information that would enable U.S. holders to make a QEF election if we are treated as a PFIC for any taxable year, and prospective investors should assume that a QEF election will not be available.

**Item 1B. Unresolved Staff Comments**

None.

**Item 2. Properties**

In August 2017, we entered into a lease agreement to consolidate our headquarters into a free standing building in New Haven, Connecticut comprising of 10,366 square feet of office space, which we began occupying during the fourth quarter of 2018. The lease had a term of 85 months and commenced on January 1, 2018, with the ability to extend to 120 months. We had the option to purchase the property for $2.7 million and exercised that option in December 2018.

We believe that our current facilities are suitable and adequate to meet our current needs. We intend to add new facilities or expand existing facilities as we add employees, and we believe that suitable additional or substitute space will be available as needed to accommodate any such expansion of our operations.

**Item 3. Legal Proceedings**

From time to time, we may be subject to litigation and claims arising in the ordinary course of business. We are not currently a party to any material legal proceedings, and we are not aware of any pending or threatened legal proceeding against us that we believe could have a material adverse effect on our business, operating results, cash flows or financial condition.

**Item 4. Mine Safety Disclosures**

Not applicable.

**PART II**

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

**Market Information**

Our common shares began trade on the New York Stock Exchange under the symbol "BHVN". The last reported sale price of our common shares on the NYSE on February 26, 2019 was $44.13 per share.

**Stock Performance Graph**


* $100 invested on May 4, 2017 in stock or index, including reinvestment of dividends. Fiscal year ending December 31.

**Shareholders**

As of February 26, 2019, there were 59 shareholders of record of our common shares. The actual number of holders of our common shares is greater than this number of record holders, and includes shareholders who are beneficial owners, but whose shares are held in street name by brokers or held by other nominees. This number of holders of record also does not include shareholders whose shares may be held in trust by other entities.

**Dividend Policy**

We have never declared or paid dividends on our share capital. We do not anticipate paying any dividends on our share capital in the foreseeable future. We currently intend to retain all available funds and any future earnings to fund the development and growth of our business. Any future determination to declare dividends will be subject to the discretion of our board of directors and will depend on various factors, including applicable laws, our results of operations, financial condition, future prospects and any other factors deemed relevant by our board of directors.

**Recent Sales of Unregistered Securities**

Not applicable.

**Issuer Purchases of Equity Securities**

We did not purchase any of our registered equity securities during the period covered by this Annual Report.

**Use of Proceeds from Registered Securities**

Not applicable.

**Item 6. Selected Consolidated Financial Data**

We have derived the consolidated statement of operations data for the years ended December 31, 2018, 2017 and 2016 and the consolidated balance sheet data as of December 31, 2018 and 2017 from our audited consolidated financial statements appearing at the end of this Annual Report on Form 10-K. The consolidated statement of operations data for the year ended December 31, 2015 and the consolidated balance sheet data as of December 31, 2016 and 2015 was derived from our historical audited consolidated financial statements not included in this Annual Report on Form 10-K.

| | Year Ended December 31, | | | |
|---|---|---|---|---|
| | 2018 | 2017 | 2016 | 2015 |
| | (in thousands) | | | |
| **Statement of Operations Data:** | | | | |
| Operating expenses: | | | | |
| Research and development[1] | $ 189,951 | $ 89,441 | $ 55,529 | $ 7,559 |
| General and administrative[1] | 34,603 | 18,141 | 5,109 | 2,137 |
| Total operating expenses | 224,554 | 107,582 | 60,638 | 9,696 |
| Loss from operations | (224,554) | (107,582) | (60,638) | (9,696) |
| Other income (expense): | | | | |
| Interest expense | (38) | (906) | (385) | — |
| Non-cash interest expense on liability related to sale of future royalties | (11,726) | — | — | — |
| Change in fair value of warrant liability | (1,182) | (3,241) | 154 | — |
| Change in fair value of derivative liability | — | 512 | (65) | (370) |
| Change in fair value of contingent equity liability | — | (13,082) | (2,263) | — |
| Loss from equity method investment | (2,808) | (1,885) | (247) | — |
| Other | (147) | — | — | — |
| Total other income (expense), net | (15,901) | (18,602) | (2,806) | (370) |
| Loss before provision for income taxes | (240,455) | (126,184) | (63,444) | (10,066) |
| Provision for income taxes | 467 | 1,006 | 90 | — |
| Net loss and comprehensive loss | (240,922) | (127,190) | (63,534) | (10,066) |
| Net loss attributable to non-controlling interests | — | — | 143 | (4) |
| Accretion of beneficial conversion feature on Series A preferred shares | — | (12,006) | — | — |
| Net loss attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd. | $ (240,922) | $ (139,196) | $ (63,677) | $ (10,062) |
| Net loss per share attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd.—basic and diluted | $ (6.15) | $ (5.00) | $ (5.05) | $ (0.91) |
| Weighted average common shares outstanding—basic and diluted | 39,188,458 | 27,845,576 | 12,608,366 | 11,009,277 |

(1) Includes non-cash stock-based compensation expense, as follows:

| | Year Ended December 31, | | | |
|---|---|---|---|---|
| | 2018 | 2017 | 2016 | 2015 |
| | (in thousands) | | | |
| Research and development | $ 8,371 | $ 6,933 | $ 2,382 | $ 1,527 |
| General and administrative | 8,554 | 6,306 | 2,221 | 1,310 |
| | $ 16,925 | $ 13,239 | $ 4,603 | $ 2,837 |

| | As of December 31, | | | |
|---|---|---|---|---|
| | 2018 | 2017 | 2016 | 2015 |
| | (in thousands) | | | |
| **Consolidated Balance Sheet Data:** | | | | |
| Cash | $ 264,249 | $ 131,468 | $ 23,565 | $ 1,460 |
| Working capital[1] | 252,805 | 127,236 | 16,093 | 1,558 |
| Total assets | 290,012 | 146,888 | 27,017 | 1,892 |
| Notes payable, net of discount | — | — | 4,216 | — |
| Accounts payable | 10,752 | 4,721 | 746 | — |
| Accrued expenses | 8,782 | 4,708 | 2,980 | — |
| Non-recourse debt related to sale of future royalties, net | 117,515 | — | — | — |
| Warrant liability | — | 4,021 | 780 | — |
| Derivative liability | — | — | 512 | — |
| Contingent equity liability, non-current | — | — | 18,938 | — |
| Notes payable to related parties | — | — | 595 | — |
| Convertible preferred shares | — | — | 43,270 | — |
| Total shareholders' equity | 150,920 | 131,971 | (45,033) | 1,087 |

(1) We define working capital as current assets less current liabilities.

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

*You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K, or this Annual Report. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors. We discuss factors that we believe could cause or contribute to these differences below and elsewhere in this report, including those set forth under Item 1A. "Risk Factors" and under "Cautionary Note Regarding Forward-Looking Statements" in this Annual Report.*

**Overview**

We are a clinical-stage biopharmaceutical company with a portfolio of innovative, late-stage product candidates targeting neurological diseases, including rare disorders. Our product candidates are small molecules based on three distinct mechanistic platforms — calcitonin gene-related peptide ("CGRP"), receptor antagonists, glutamate modulators and myeloperoxidase, or MPO, inhibition — which we believe have the potential to significantly improve existing treatment approaches across a diverse set of neurological indications with high unmet need in both large markets and orphan indications. Our programs include the following:

| Product | Platform | Indication | Development Stage |
|---|---|---|---|
| Rimegepant | CGRP | Acute treatment and prevention of migraine | Three pivotal Phase 3 trials for acute treatment complete; long-term safety ongoing. Trial for prevention initiated in the fourth quarter of 2018. NDA submissions for Zydis ODT and tablet formulations for acute treatment anticipated in the second quarter of 2019. |
| BHV-3500 | CGRP | Acute treatment and prevention of migraine | Phase 1 complete. Phase 2/3 trial expected to begin in first quarter of 2019. |
| Troriluzole | Glutamate | Ataxias | Phase 2/3 randomization phase in SCA complete; Extension trial ongoing. Phase 3 trial to begin in second quarter of 2019. |
| Troriluzole | Glutamate | Obsessive Compulsive Disorder (“OCD”) | Phase 2/3 ongoing. |
| Troriluzole | Glutamate | Alzheimer’s disease | Phase 2/3 ongoing. |
| Troriluzole | Glutamate | Generalized Anxiety Disorder ("GAD") | Phase 2/3 ongoing. |
| BHV-0223 | Glutamate | Amyotrophic Lateral Sclerosis (“ALS”) | NDA filed with FDA in fourth quarter of 2018. Prescription Drug User Fee Act ("PDUFA") date of July 21, 2019. |
| BHV-5000 | Glutamate | Neuropsychiatric disorders | Phase 1 trial completed 2018; Additional nonclinical studies anticipated for 2019. |
| Verdiperstat | MPO | Neuroinflammation | Phase 3 trial for the treatment of multiple system atrophy ("MSA") expected to begin in third quarter of 2019. |

**CGRP Platform**

*Study 301/Study 302*

The most advanced product candidate from our CGRP receptor antagonist platform is rimegepant, an orally available, potent and selective small molecule human CGRP receptor antagonist that we are developing for the acute and preventive treatment of migraine. In March 2018, we announced positive topline data from our first two pivotal Phase 3 trials ("Study 301" and "Study 302") for the acute treatment of migraine.

*Study 303*

On December 3, 2018, we announced positive topline data from a randomized, controlled Phase 3 clinical trial ("BHV3000-303" or "Study 303") evaluating the efficacy and safety of our Zydis ODT formulation of rimegepant for the acute treatment of migraine. Additional secondary and exploratory outcome measures from this study are anticipated to be presented at upcoming scientific meetings in 2019. The co-primary endpoints achieved in the Phase 3 trials are consistent with regulatory guidance from the U.S. Food and Drug Administration ("FDA"), and provide the basis for planned submissions of new drug

applications ("NDA"), to the FDA for the Zydis ODT and tablet formulations in 2019. If either NDA is approved by the FDA, we expect to launch rimegepant in 2020.

*Long-term Safety Study*

On December 10, 2018, we announced the results of an interim analysis from our ongoing long-term safety study ("BHV3000-201" or "Study 201"). In addition to the interim safety analysis, preliminary exploratory open-label efficacy data from Study 201 suggest that rimegepant may be associated with a reduction in migraine days per month (30 days) compared to the observational lead-in period, suggesting a potential preventive effect that warrants further study. We initiated a double-blind, placebo-controlled trial examining regularly scheduled dosing of rimegepant 75mg for the preventive treatment of migraine in November 2018. Subjects will continue to participate in Study 201 with additional data analyses to be submitted to the FDA in connection with the planned NDA submissions, including the required 120-day safety update.

*Additional Clinical Trials*

In November 2017, the FDA agreed to our initial acute treatment pediatric study plan. In February 2018, a request for scientific advice for rimegepant was submitted to the Committee for Medicinal Products for Human Use ("CHMP"), a committee of the European Medicines Agency ("EMA"), and feedback was received in June 2018. Based on this feedback, we believe we have several potential pathways to approval.

A fourth Phase 3 clinical trial to evaluate the efficacy and safety of rimegepant as a preventive therapy for migraine was initiated in the fourth quarter 2018.

*BHV-3500*

Administration of intranasal BHV-3500 in a Phase 1 clinical trial was initiated in October 2018 and has achieved targeted therapeutic exposures. The compound is expected to advance into a Phase 2/3 trial to evaluate efficacy for the acute treatment of migraine in the first quarter of 2019. We believe that intranasal BHV-3500 may provide an ultra-rapid onset of action that could be used in a complimentary fashion with other migraine treatment when the speed of onset is critical to a patient.

**Glutamate Platform**

We are developing three product candidates that modulate the body's glutamate system. Two of these product candidates, troriluzole, previously referred to as trigriluzole or BHV-4157, and BHV-0223, act as glutamate transporter modulators, while our product candidate BHV-5000 is an antagonist of the glutamate N-methyl-D-aspartate ("NMDA"), receptor.

*Troriluzole for Ataxias*

We are developing troriluzole for the treatment of ataxias; our initial focus has been spinocerebellar ataxia ("SCA"). We have received both orphan drug designation and fast track designation from the FDA for troriluzole for the treatment of SCA. We plan to initiate a second randomized, controlled trial in the second quarter of 2019 to further evaluate the efficacy of troriluzole in SCA. The clinical observations from our Phase 2/3 trial and open-label extension phase in SCA support our decision to advance troriluzole into an additional randomized, controlled trial that could provide the data needed to serve as the basis for an NDA.

*Troriluzole for Other Indications*

A Phase 2/3 double-blind, randomized, controlled trial to assess the efficacy of troriluzole in obsessive compulsive disorder, or OCD, commenced in December 2017. We expect to complete the randomization of this trial by the end of 2019. In addition, a Phase 2/3 double-blind, randomized, controlled trial of troriluzole in the treatment of mild-to-moderate Alzheimer's disease has advanced with the Alzheimer's Disease Cooperative Study, a consortium of sites funded by the National Institutes of Health. In July 2018, we received authorization to proceed from the FDA and subsequently commenced the trial. We expect to complete enrollment and announce interim futility results for this trial in the fourth quarter of 2019. We began enrollment in a Phase 2/3 clinical trial of troriluzole in GAD in February 2019 and expect to complete enrollment of this trial by the end of 2019.

*BHV-0223*

We are developing BHV-0223 for the treatment of ALS. In January 2018, we announced positive results of a bioequivalence study with BHV-0223 and marketed riluzole, thus providing pivotal data that we believe are sufficient for the filing of an NDA with the FDA, allowing us to pursue the regulatory approval of BHV-0223 for ALS under Section 505(b)(2) of the U.S. Federal Food, Drug, and Cosmetic Act. An NDA was submitted in September 2018 and the PDUFA data is in July 2019.

*BHV-5000*

We are also developing BHV-5000, an orally available, first-in-class, low-trapping NMDA receptor antagonist, for the treatment of neuropsychiatric diseases. One potential target indication includes Complex Regional Pain Syndrome ("CRPS"). CRPS is a rare, chronic pain condition typically affecting limbs and triggered by traumatic injury. Accompanying symptoms also include chronic inflammation and reduced mobility in the affected areas. Other disorders of interest include treatment-resistant major depressive disorder and Rett syndrome. Rett syndrome is a rare and severe genetic neurodevelopmental disorder for which no approved treatments are currently available. We acquired worldwide rights to BHV-5000 under an exclusive license agreement with AstraZeneca AB in October 2016. We selected a lead formulation at the end of 2017 and completed single dosing in a Phase 1 clinical trial of BHV-5000 in January 2018 to evaluate its pharmacokinetic properties. Nonclinical studies are ongoing to support future trials.

**MPO Platform**

*Verdiperstat*

We are developing verdiperstat (previously BHV-3241), an oral myeloperoxidase inhibitor for the treatment of MSA, a rare, rapidly progressive and fatal neurodegenerative disease with no cure or effective treatments. Verdiperstat was progressed through Phase 2 clinical trials by AstraZeneca AB. We have entered into an exclusive license agreement with AstraZeneca AB for the product candidate and, after reactivating the IND, plan to initiate a Phase 3 clinical trial of verdiperstat for the treatment of MSA in the third quarter2019. In February 2019, we received orphan drug designation from the FDA for the treatment of MSA. Verdiperstat has also received orphan drug designation for the treatment of MSA from the European Commission upon recommendation from the European Medicines Agency's Committee for Orphan Medicinal Products.

**Financings and Other Recent Developments**

Since our inception, we have not generated any revenue and have incurred significant operating losses and negative cash flows from our operations. We have funded our operations primarily with proceeds from sales of equity, and other financing transactions. Subsequent to our initial public offering ("IPO"), we raised funds through sales of our equity in private placements, as well as through the sale of a revenue participation right related to future royalties.

In May 2017, our registration statement on Form S-1 relating to our IPO was declared effective by the SEC. The IPO closed on May 9, 2017 and we issued and sold 9,900,000 common shares at a public offering price of $17.00 per share, resulting in net proceeds of $152.7 million after deducting underwriting discounts and commissions and other offering expenses. In addition, on May 9, 2017, the underwriters of our IPO fully exercised their option to purchase additional shares, and on May 11, 2017, we issued and sold an additional 1,485,000 common shares, resulting in additional net proceeds to us of $23.5 million, after deducting underwriting discounts and commissions and other offering expenses. The aggregate net proceeds we received from the IPO, after deducting underwriting discounts and commissions and offering expenses, were $176.1 million.

In March 2018, we sold an aggregate of 2,000,000 common shares in a private placement at a price of $27.50 per share, for net proceeds of $52.0 million after deducting underwriting discounts and commissions of $2.8 million and other offering expenses of $0.2 million. Subsequent to the closing of the Private Placement, we paid BMS the $50.0 million upfront payment under the BMS Amendment.

In June 2018, we entered into a funding agreement ("Funding Agreement") to sell tiered, sales-based royalty rights on global net sales of the pharmaceutical products containing the compounds rimegepant or BHV-3500 and certain derivative compounds thereof ("Products") to RPI Finance Trust ("RPI"). We issued to RPI the right to receive certain revenue participation payments, subject to certain reductions, based on the future global net sales of the Products, for each calendar quarter during the royalty term contemplated by the Funding Agreement, in exchange for $100.0 million in cash. Specifically, the participation rate commences at 2.1 percent on annual global net sales of up to and equal to $1.5 billion, declining to 1.5 percent on annual global net sales exceeding $1.5 billion.

Concurrently, we entered into a common stock purchase agreement with RPI, pursuant to which we issued and sold 1,111,111 common shares to RPI. RPI paid $45.00 per share, resulting in net proceeds of $49.9 million after deducting offering expenses of $0.1 million.

In December 2018, we closed on an underwritten public offering of 3,859,060 common shares, including the full exercise of the underwriters' option to purchase additional shares, at a price to the public of $37.25 per share. The aggregate net proceeds to us from the offering, after deducting the underwriting discounts and commissions and offering expenses payable, were approximately $134.5 million.

As of December 31, 2018, we had cash of $264.2 million. Cash in excess of immediate requirements is invested in non-interest-bearing accounts with a view to liquidity and capital preservation. We believe that our cash as of December 31, 2018 will enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 months. We have based these estimates on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner

than we expect. See "—Liquidity and Capital Resources." Our future viability beyond that point is dependent on our ability to raise additional capital to finance our operations.

**Components of Our Results of Operations**

***Revenue***

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the near future. If our development efforts for our product candidates are successful and result in regulatory approval or additional license agreements with third parties, we may generate revenue in the future from product sales.

***Operating Expenses***

*Research and Development Expenses*

Research and development expenses consist primarily of costs incurred in connection with the development of our product candidates. We expense research and development costs as incurred. These expenses include:

- expenses incurred under agreements with contract research organizations ("CROs") or contract manufacturing organizations ("CMOs"), as well as investigative sites and consultants that conduct our clinical trials, preclinical studies and other scientific development services;
- manufacturing scale-up expenses and the cost of acquiring and manufacturing preclinical and clinical trial materials and commercial materials, including manufacturing validation batches;
- employee-related expenses, including salaries, benefits, travel and non-cash share-based compensation expense for employees engaged in research and development functions;
- costs related to compliance with regulatory requirements;
- payments made in cash, equity securities or other forms of consideration under third-party licensing agreements.

We recognize external development costs based on an evaluation of the progress to completion of specific tasks using estimates of our clinical personnel or information provided to us by our service providers.

Our external direct research and development expenses are tracked on a program-by-program basis for our product candidates and consist primarily of external costs, such as fees paid to outside consultants, CROs, contract manufacturing organizations, and central laboratories in connection with our preclinical development, process development, manufacturing and clinical development activities. Our direct research and development expenses by program also include fees incurred under license agreements. We do not allocate employee costs or other indirect costs, to specific programs because these costs are deployed across multiple programs and, as such, are not separately classified. We use internal resources primarily to oversee the research and development as well as for managing our preclinical development, process development, manufacturing and clinical development activities. Many employees work across multiple programs, and we do not track personnel costs by program.

Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. As a result, we expect that our research and development expenses will increase over the next several years as we increase personnel costs conduct clinical trials and prepare regulatory filings for our product candidates. We also expect to incur additional expenses related to milestone and royalty payments payable to third parties with whom we have entered into license agreements to acquire the rights to our product candidates.

The successful development and commercialization of our product candidates is highly uncertain. At this time, we cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the preclinical and clinical development of any of our product candidates or when, if ever, material net cash inflows may commence from any of our product candidates. This uncertainty is due to the numerous risks and uncertainties associated with product development and commercialization, including the uncertainty of:

- the scope, progress, outcome and costs of our preclinical development activities, clinical trials and other research and development activities;
- establishment of an appropriate safety profile with IND-enabling studies;
- successful patient enrollment in, and the initiation and completion of, clinical trials;
- the timing, receipt and terms of any marketing approvals from applicable regulatory authorities;
- establishment of commercial manufacturing capabilities or making arrangements with third-party manufacturers;

- development and timely delivery of commercial-grade drug formulations that can be used in our clinical trials and for commercial launch;
- acquisition, maintenance, defense and enforcement of patent claims and other intellectual property rights;
- significant and changing government regulation;
- initiation of commercial sales of our product candidates, if and when approved, whether alone or in collaboration with others; and
- maintenance of a continued acceptable safety profile of the product candidates following approval.

*General and Administrative Expenses*

General and administrative expenses include salaries, benefits, travel expense and non-cash share-based compensation expense for personnel in executive, finance and administrative functions. General and administrative expenses also include professional fees for legal, patent, consulting, accounting and audit services.

We anticipate that our general and administrative expenses will increase in the future as we increase our general and administrative headcount to support our continued research and development activities of our product candidates. We also continue to incur accounting, audit, legal, regulatory, compliance, public relations, director and insurance costs associated with being a public company. Additionally, if and when we believe a regulatory approval of a product candidate appears likely, we expect an increase in payroll and related expenses as a result of our preparation for commercial operations, especially as it relates to the sales and marketing of our product candidate.

***Other Income (Expense)***

*Change in Fair Value of Warrant Liability*

In connection with entering into a credit agreement, we issued warrants to purchase common shares to two of our directors in connection with a guarantee of our obligations under the agreement. We previously classified the warrants as a liability on our consolidated balance sheet because each warrant represented a freestanding financial instrument that was not indexed to our shares. The warrant liability was initially recorded at fair value upon entering into the credit agreement and was subsequently remeasured to fair value at each reporting date. Changes in the fair value of the warrant liability were recognized as a component of other income (expense), net in the consolidated statement of operations and comprehensive loss. On January 26, 2018, the anti-dilution price protection provisions contained within the warrants expired. Due to the expiration of these provisions, we discontinued classification of these warrants as a liability, and have accordingly reclassified them to additional paid-in capital within shareholders' equity.

*Loss from Equity Method Investment*

From August 2016 through December 2018, we purchased shares of common stock in Kleo Pharmaceuticals, Inc., a privately held Delaware corporation (“Kleo”) in a series of transactions. As of December 31, 2018 and 2017, we owned approximately 41.9% and 43.3%, respectively, of the outstanding shares of Kleo’s common stock. We account for our investment in Kleo under the equity method of accounting. As a result, our proportionate share of Kleo’s net income or loss each reporting period is included in other income (expense), net, in our consolidated statement of operations and comprehensive loss and results in a corresponding adjustment to the carrying value of the equity method investment on our consolidated balance sheet.

*Non-Cash Interest Expense on Liability Related to Sale of Future Royalties*

We have accounted for the Funding Agreement with RPI as a liability financing. The debt is amortized under the effective interest rate method and, accordingly, we are recording non-cash interest expense over the estimated term of the Funding Agreement. The liability related to sale of future royalties, and the debt amortization, are based on our current estimate of future royalties expected to be paid over the term of the Funding Agreement. These estimates include projections we make and projections from outside the Company and involve significant judgment and involve inherent uncertainties. We will periodically assess the expected royalty payments and, if materially different than our previous estimate, will prospectively adjust and recognize the related non-cash interest expense. The transaction costs associated with the liability will be amortized to non-cash interest expense over the estimated term of the Funding Agreement.

***Provision for Income Taxes***

As a company incorporated in the British Virgin Islands (“BVI”), we are principally subject to taxation in the BVI. Under the current laws of the BVI, tax on a company’s income is assessed at a zero percent tax rate. As a result, we have not recorded any income tax benefits from losses incurred in the BVI during each reporting period, and no net operating loss carryforwards will be available to us for those losses. We have historically outsourced all of the research and clinical development for our programs under a master services agreement with our wholly owned subsidiary, Biohaven Pharmaceuticals, Inc., a Delaware corporation (“BPI”). As a result of providing services under this agreement, BPI was profitable during the twelve months ended December 31, 2018, 2017 and 2016, and BPI is subject to taxation in the United States. Our provision for income taxes has

historically been comprised of Federal alternative minimum tax, and state taxes through December 31, 2017, and federal tax due to general business credit limitations and state taxes in 2018.

As of December 31, 2018, we evaluated our deferred tax assets and determined that a full valuation allowance on these assets was appropriate due to excess credits.

**Results of Operations**

***Comparison of the Years Ended December 31, 2018 and 2017***

The following table summarizes our results of operations for the years ended December 31, 2018 and 2017:

| | Year Ended December 31, | | Change |
|---|---|---|---|
| | 2018 | 2017 | |
| | | (in thousands) | |
| Operating expenses: | | | |
| Research and development | $ 189,951 | $ 89,441 | $ 100,510 |
| General and administrative | 34,603 | 18,141 | 16,462 |
| Total operating expenses | 224,554 | 107,582 | 116,972 |
| Loss from operations | (224,554) | (107,582) | (116,972) |
| Other income (expense): | | | |
| Interest expense | (38) | (906) | 868 |
| Non-cash interest expense on liability related to sale of future royalties | (11,726) | — | (11,726) |
| Change in fair value of warrant liability | (1,182) | (3,241) | 2,059 |
| Change in fair value of derivative liability | — | 512 | (512) |
| Change in fair value of contingent equity liability | — | (13,082) | 13,082 |
| Loss from equity method investment | (2,808) | (1,885) | (923) |
| Other | (147) | — | (147) |
| Total other income (expense), net | (15,901) | (18,602) | 2,701 |
| Loss before provision for income taxes | (240,455) | (126,184) | (114,271) |
| Provision for income taxes | 467 | 1,006 | (539) |
| Net loss and comprehensive loss | (240,922) | (127,190) | $ (113,732) |
| Accretion of beneficial conversion feature on Series A preferred shares | — | (12,006) | 12,006 |
| Net loss attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd. | (240,922) | (139,196) | $ (101,726) |

*Research and Development Expenses*

| | Year Ended December 31, | | Change |
|---|---|---|---|
| | 2018 | 2017 | |
| | | (in thousands) | |
| Direct research and development expenses by program: | | | |
| BHV-0223 | $ 6,134 | $ 3,950 | $ 2,184 |
| Troriluzole | 13,222 | 13,139 | 83 |
| Rimegepant | 75,719 | 48,122 | 27,597 |
| BHV-3500 | 11,241 | 5,728 | 5,513 |
| BHV-5000 | 2,147 | 1,918 | 229 |
| Unallocated research and development costs: | | | |
| Personnel related (including non-cash share-based compensation) | 19,882 | 14,304 | 5,578 |
| BMS Amendment upfront license payment | 50,000 | — | 50,000 |
| Other | 11,606 | 2,280 | 9,326 |
| Total research and development expenses | $ 189,951 | $ 89,441 | $ 100,510 |

Research and development expenses were $190.0 million for the year ended December 31, 2018, compared to $89.4 million for the year ended December 31, 2017. The increase of $100.5 million was primarily due to an increase of $50.0 million due to the BMS Amendment upfront payment, $27.6 million in direct costs for our rimegepant program, $5.6 million in

personnel costs, $5.5 million in direct costs for our BHV-3500 program, $2.2 million in direct costs for our BHV-0223 program and $9.3 million in unallocated external costs.

The increases in direct costs for our rimegepant and BHV-0223 programs were primarily due to an increase in the number of clinical trials during the year ended December 31, 2018. The increase in costs for BHV-3500 was primarily a result of further clinical development and advancement of the programs compared to the prior period.

The increase in personnel costs of $5.6 million was primarily a result of hiring additional research and development personnel. Our headcount in research and development increased to 41 as of December 31, 2018, compared to 29 as of December 31, 2017. Non-cash share-based compensation expense, included in personnel-related costs, was $8.4 million for the year ended December 31, 2018 compared to $6.9 million for the year ended December 31, 2017, an increase of $1.4 million.

*General and Administrative Expenses*

General and administrative expenses were $34.6 million for the year ended December 31, 2018, compared to $18.1 million for the year ended December 31, 2017. The increase of $16.5 million was primarily due to increases in personnel-related costs, including non-cash share-based compensation, due to the hiring of additional personnel in our general and administrative functions, preparation for commercialization activities, professional fees supporting ongoing business operations, and additional costs to comply with requirements of operating as a public company. Our headcount, excluding of research and development personnel, increased to 22 as of December 31, 2018 compared to 13 as of December 31, 2017. Non-cash share-based compensation expense, included in personnel-related costs, was $8.6 million for the year ended December 31, 2018, an increase of $2.3 million as compared to the same period in 2017.

*Other Income (Expense),* Net

Other income (expense), net was a net expense of $15.9 million for the year ended December 31, 2018, compared to net expense of $18.6 million for the year ended December 31, 2017. The decrease of $2.7 million in net expense was primarily due to a $13.1 million decrease in fair value of the contingent equity liabilities associated with our license agreements with BMS and AstraZeneca in 2017, which did not occur in 2018, and a $2.1 million larger decrease in fair value of the warrant liabilities associated with the warrants issued in connection with our Wells Fargo credit agreement during 2017 compared to 2018, which was satisfied upon our initial public offering in May 2017 ("IPO"), mostly offset by an increase in the expense related to the non-cash interest expense on our liability related to the sale of future royalties of $11.7 million.

*Provision for Income Taxes*

We recorded a provision for income taxes of $0.5 million for the year ended December 31, 2018, compared to $1.0 million for the year ended December 31, 2017. We recorded a tax provision for the year ended December 31, 2018 for the state income taxes of BPI's profitable operations in the United States during that period and federal income taxes due to general business credit limitations. Due to tax reform enacted in the United States in December 2017, we are no longer subject to the alternative minimum tax.

***Comparison of the Years Ended December 31, 2017 and December 31, 2016***

The following table summarizes our results of operations for the years ended December 31, 2017 and December 31, 2016:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2017 | 2016 | Change |
| | | (in thousands) | |
| Operating expenses: | | | |
| Research and development | $ 89,441 | $ 55,529 | $ 33,912 |
| General and administrative | 18,141 | 5,109 | 13,032 |
| Total operating expenses | 107,582 | 60,638 | 46,944 |
| Loss from operations | (107,582) | (60,638) | (46,944) |
| Other income (expense): | | | |
| Interest expense | (906) | (385) | (521) |
| Change in fair value of warrant liability | (3,241) | 154 | (3,395) |
| Change in fair value of derivative liability | 512 | (65) | 577 |
| Change in fair value of contingent equity liability | (13,082) | (2,263) | (10,819) |
| Loss from equity method investment | (1,885) | (247) | (1,638) |
| Total other income (expense), net | (18,602) | (2,806) | (15,796) |
| Loss before provision for income taxes | (126,184) | (63,444) | (62,740) |
| Provision for income taxes | 1,006 | 90 | 916 |
| Net loss and comprehensive loss | $ (127,190) | $ (63,534) | $ (63,656) |
| Net income attributable to non-controlling interests | — | 143 | (143) |
| Accretion of beneficial conversion feature on Series A preferred shares | (12,006) | — | (12,006) |
| Net loss attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd. | $ (139,196) | $ (63,677) | $ (75,519) |

*Research and Development Expenses*

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2017 | 2016 | Change |
| | | (in thousands) | |
| Direct research and development expenses by program: | | | |
| BHV-0223 | $ 3,950 | $ 380 | $ 3,570 |
| Troriluzole | 13,139 | 11,761 | 1,378 |
| Rimegepant | 48,122 | 25,139 | 22,983 |
| BHV-3500 | 5,728 | — | 5,728 |
| BHV-5000 | 1,918 | 13,550 | (11,632) |
| Unallocated research and development costs: | | | |
| Personnel related (including non-cash share-based compensation) | 14,304 | 4,137 | 10,167 |
| Other | 2,280 | 562 | 1,718 |
| Total research and development expenses | $ 89,441 | $ 55,529 | $ 33,912 |

Research and development expenses were $89.4 million for the year ended December 31, 2017, compared to $55.5 million for the year ended December 31, 2016. The increase of $33.9 million was primarily due to increases of $11.9 million in personnel and unallocated external costs, $23.0 million in direct costs for our rimegepant program, $5.7 million in direct costs for our BHV-3500 program, $3.6 million in direct costs for our BHV-0223 program, partially offset by a decrease of $11.6 million in direct costs for our BHV-5000 program.

The increase in direct costs for rimegepant was primarily due to costs of Phase 3 trials, long-term safety study and related drug supply, as well as a $5.0 million payment to BMS upon initiation of our Phase 3 trial. The increase in costs for BHV-3500 were primarily related to formulation development and toxicology for this program. The increases in direct costs for our BHV-0223 program was primarily a result of our bioequivalence study for this program.

The decrease in direct costs for our BHV-5000 program during 2017 primarily related to the costs associated with acquiring technology under our licensing agreement with AstraZeneca in October 2016 which did not recur in 2017. Upon acquiring the technology, we accrued a liability of $8.6 million for our contingent obligation to issue equity to AstraZeneca and paid an upfront license fee of $5.0 million under the agreement, for total expense of $13.6 million during the year ended December 31, 2016. During the year ended December 31, 2017, we incurred direct costs of $1.9 million primarily associated with pre-clinical studies which commenced in the second quarter of 2017 and start-up activities related to our Phase 1 clinical trial which commenced in the fourth quarter of 2017.

The increase in personnel costs of $10.2 million in personnel-related costs was primarily as a result of hiring additional personnel to support our expanding number of clinical trials and preparing for potential commercialization of BHV-0223. Our headcount in research and development increased to 29 as of December 31, 2017, compared to 6 as of December 31, 2016. Personnel-related costs for the years ended December 31, 2017 and 2016 included non-cash share-based compensation expense of $6.9 million and $2.4 million, respectively. The increase in non-cash share-based compensation was a result of hiring new personnel and the impact of higher stock price on both our employee and non-employee non-cash share-based compensation expense.

The increase in other unallocated costs was primarily due to increased use of research and development consultants that support activities across multiple drug candidate programs as well as the increased purchase of supplies used across all programs.

*General and Administrative Expenses*

General and administrative expenses were $18.1 million for the year ended December 31, 2017, compared to $5.1 million for the year ended December 31, 2016. The increase of $13.0 million was primarily due to increases of $5.9 million in personnel-related costs, including non-cash share-based compensation, due to the hiring of additional personnel in our general and administrative functions, $5.8 million in professional fees supporting ongoing business operations, including increased compliance and other costs associated with becoming a public company. Personnel-related costs for the years ended December 31, 2017 and 2016 included non-cash share-based compensation expense of $6.3 million and $2.2 million, respectively. The increase in non-cash share-based compensation was a result of hiring new personnel and the impact of higher stock price on both our employee and non-employee non-cash share-based compensation expense.

*Other Income (Expense), Net*

Other income (expense), net was a net expense of $18.6 million for the year ended December 31, 2017, compared to net expense of $2.8 million for the year ended December 31, 2016. The increase of $15.8 million in net expense was primarily due to an increase of $10.8 million in the fair value of the contingent equity liabilities associated with our license agreements with BMS and AstraZeneca, an increase of $3.4 million in fair value of the warrant liabilities associated with the warrants issued in connection with our Wells Fargo credit agreement and an increase of $1.6 million of loss from equity method investment which also reflects the increased ownership percentage during 2017.

*Provision for Income Taxes*

We recorded a provision for income taxes of $1.0 million for the year ended December 31, 2017, compared to $0.1 million for the year ended December 31, 2016. We recorded a tax provision for the year ended December 31, 2017 for the U.S. Federal alternative minimum tax and state income taxes related to BPI's profitable operations in the United States.

**Liquidity and Capital Resources**

Since our inception, we have not generated any revenue and have incurred significant operating losses and negative cash flows from our operations. Prior to the completion of our IPO in May 2017, we funded our operations primarily with proceeds from the sale of preferred shares and common shares through private placements and borrowings under our credit agreement with Wells Fargo. Prior to the completion of our IPO, we had received net cash proceeds of $96.4 million from sales of our preferred shares and common shares and gross proceeds of $5.0 million from borrowings under the credit agreement.

On May 3, 2017, our registration statement on Form S-1 relating to our IPO was declared effective by the SEC. The IPO closed on May 9, 2017 and we issued and sold 9,900,000 common shares at a public offering price of $17.00 per share, resulting in net proceeds of $152.7 million after deducting underwriting discounts and commissions and other offering expenses. In addition, on May 9, 2017, the underwriters of our IPO fully exercised their option to purchase additional shares,

and on May 11, 2017, we issued and sold an additional 1,485,000 common shares, resulting in additional net proceeds to us of $23.5 million, after deducting underwriting discounts and commissions and other offering expenses. The aggregate net proceeds we received from the IPO, after deducting underwriting discounts and commissions and offering expenses, were $176.1 million.

In March 2018, we sold an aggregate of 2,000,000 common shares in a private placement at a price of $27.50 per share, for net proceeds of $52.0 million after deducting underwriting discounts and commissions of $2.8 million and other offering expenses of $0.2 million. Subsequent to the closing of the Private Placement, we paid BMS the $50.0 million upfront payment under the BMS Amendment.

In June 2018, we entered into the Funding Agreement to sell tiered, sales-based royalty rights on global net sales of pharmaceutical products containing the compounds rimegepant or BHV-3500 and Products to RPI. We issued to RPI the right to receive certain revenue participation payments, subject to certain reductions, based on the future global net sales of the Products, for each calendar quarter during the royalty term contemplated by the Funding Agreement, in exchange for $100.0 million in cash. Specifically, the participation rate commences at 2.10 percent on annual global net sales of up to and equal to $1.5 billion, declining to 1.50 percent on annual global net sales exceeding $1.5 billion.

Concurrently, we entered into a common stock purchase agreement with RPI, pursuant to which we issued and sold 1,111,111 common shares to RPI. RPI paid $45.00 per share, resulting in net proceeds of $49.9 million after deducting offering expenses of $0.1 million.

In December 2018, we closed on an underwritten public offering of 3,859,060 common shares, including the full exercise of the underwriters' option to purchase additional shares, at a price to the public of $37.25 per share. The aggregate net proceeds to us from the offering, after deducting the underwriting discounts and commissions and offering expenses payable, were approximately $134.5 million.

As of December 31, 2018, we had cash of $264.2 million. Cash in excess of immediate requirements is invested in non-interest-bearing accounts with a view to liquidity and capital preservation.

***Cash Flows***

The following table summarizes our cash flows for each of the periods presented:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| | | (in thousands) | |
| Net cash used in operating activities | $ (197,141) | $ (94,815) | $ (29,504) |
| Net cash used in investing activities | (10,540) | (7,168) | (3,026) |
| Net cash provided by financing activities | 340,462 | 209,759 | 54,762 |
| Net increase in cash | $ 132,781 | $ 107,776 | $ 22,232 |

*Operating Activities*

During the year ended December 31, 2018, operating activities used $197.1 million of cash, an increase of $102.3 million as compared to the year ended December 31, 2017. The increase in cash usage was primarily due to the $50.0 million upfront payment under the BMS Amendment, and increases in cash paid for clinical trials, including increases in upfront payments to CROs related to our rimegepant clinical trials, personnel, professional fees and other infrastructure costs.

During the year ended December 31, 2017, operating activities used $94.8 million of cash, resulting from our net loss of $128.0 million, including a $5.0 million payment to BMS upon commencement of our Phase 3 trial, partially offset by non-cash charges of $31.8 million and net cash provided by changes in our operating assets and liabilities of $1.4 million. Net cash provided by changes in our operating assets and liabilities for the year ended December 31, 2017 consisted primarily of a $1.4 million increase in accrued expenses and a $4.0 million increase in accounts payable partially offset by an increase of $4.0 million in prepaid expense and other current assets. The increases in accrued expenses, accounts payable and prepaid expenses and other current assets were primarily due to increases in clinical trial activities, as well as professional fees associated with the preparation, audit and review of our financial statements.

During the year ended December 31, 2016 operating activities used $29.5 million of cash, resulting from our net loss of $63.5 million, partially offset by non-cash charges of $31.2 million and net cash provided by changes in our operating assets and liabilities of $2.8 million. Net cash provided by changes in our operating assets and liabilities for the year ended December 31, 2016 consisted primarily of a $2.1 million increase in accrued expenses and a $0.7 million increase in accounts payable. The increase in accrued expenses and accounts payable was due to our increased level of operating activities and the timing of vendor invoicing and payments.

*Investing Activities*

During the year ended December 31, 2018, we used $10.5 million of cash in investing activities, an increase of $3.3 million as compared to the year ended December 31, 2017. The increase was primarily due to an increase in the amount invested for building improvements, and the purchase of our headquarters for $2.7 million, during the year ended December 31, 2018, as compared to the year ended December 31, 2017. In November 2018 we purchased 1,420,818 shares of Kleo's preferred stock for cash consideration of $5.0 million. As of December 31, 2018 our ownership in the outstanding stock of Kleo was 41.9%.

During the year ended December 31, 2017, we used $7.0 million of cash in investing activities, primarily consisting of $6.6 million of our purchases of 6,674,543 shares of Kleo common stock, comprising ownership of 43.3% ownership of Kleo, and $0.5 million of our purchases of property and equipment.

During the year ended December 31, 2016, we used $3.2 million of cash in investing activities, primarily consisting of our initial purchase of 3,000,000 shares of Kleo common stock.

*Financing Activities*

During the year ended December 31, 2018, net cash provided by financing activities was $340.5 million, an increase of $130.7 million compared to the year ended December 31, 2017. The increase was primarily due to an increase in funds raised through equity offerings and sales of future royalties, proceeds from the exercise of stock options, and a decrease in the amount of offering costs paid in the year ended December 31, 2018, as compared to the year ended December 31, 2017.

During the year ended December 31, 2017, net cash provided by financing activities was $209.8 million, primarily consisting of net proceeds of $176.1 million from our issuance of common shares in our IPO and $38.6 million from our issuance of Series A preferred shares, partially offset by our repayment of notes payable of $5.0 million in connection with the Wells Fargo credit agreement.

During the year ended December 31, 2016, net cash provided by financing activities was $54.8 million, primarily consisting of $38.6 million in net proceeds from our issuance of Series A preferred shares, $11.3 million in net proceeds from our issuance of common shares and $5.0 million in proceeds from our Wells Fargo credit agreement.

***Funding Requirements***

We expect our expenses to increase in connection with our ongoing activities, particularly as we advance the preclinical activities and clinical trials of our product candidates. Our costs will also increase as we:

- Complete our ongoing long-term safety study of rimegepant, Phase 1 supporting trials of rimegepant and our ongoing Phase 3 clinical trial to evaluate rimegepant as a preventive therapy for migraine;
- complete the ongoing extension phase of the Phase 2/3 clinical trial of troriluzole in SCA and our ongoing Phase 2/3 trials of troriluzole in OCD, Alzheimer's disease and GAD and, conduct a second randomized controlled trial to assess the efficacy of troriluzole in SCA;
- conduct support activities for future clinical trials of BHV-5000;
- conduct our planned Phase 2/3 clinical trial of BHV-3500 and related support activities;
- conduct our planned Phase 3 clinical trial of verdiperstat in multiple system atrophy;
- continue to initiate and progress other supporting studies required for regulatory approval of our product candidates, including long-term safety studies, drug-drug interaction studies, preclinical toxicology and carcinogenicity studies;
- make required milestone and royalty payments under the license agreements by which we acquired some of the rights to our product candidates;
- make required royalty payments to RPI under the Funding Agreement;
- initiate preclinical studies and clinical trials for any additional indications for our current product candidates and any future product candidates that we may pursue;
- continue to build our portfolio of product candidates through the acquisition or in-license of additional product candidates or technologies;
- continue to develop, maintain, expand and protect our intellectual property portfolio;

- pursue regulatory approvals for our current and future product candidates that successfully complete clinical trials, including rimegepant and BHV-0223;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any product candidate for which we may obtain marketing approval;
- hire additional clinical, medical, commercial, and development personnel; and
- incur additional legal, accounting and other expenses in operating as a public company.

We expect that our existing cash will be sufficient to fund our planned operating expenses, financial commitments and other cash requirements into the fourth quarter of 2020. The assumption for cash usage through this date assumes that planned programs and expenditures continue and that we do not reduce, stop or curtail programs or other spending. Beyond that point, we will need to raise additional capital to finance our operations, which cannot be assured.

We have based these estimates on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect. We expect that we will require additional capital to commercialize rimegepant, if we receive regulatory approval, and to pursue in-licenses or acquisitions of other product candidates. If we receive regulatory approval for rimegepant, troriluzole, BHV-0223, or our other product candidates, we expect to incur commercialization expenses related to product manufacturing, sales, marketing and distribution, depending on where we choose to commercialize or whether we commercialize jointly or on our own.

Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical product candidates, we are unable to estimate the exact amount of our working capital requirements. Our future funding requirements will depend on and could increase significantly as a result of many factors, including:

- the scope, progress, results and costs of researching and developing our product candidates, and conducting preclinical studies and clinical trials;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of future activities, including product sales, medical affairs, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sale of our products, should any of our product candidates receive marketing approval;
- the costs and timing of hiring new employees to support our continued growth;
- the costs of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other product candidates and technologies;
- the costs of manufacturing commercial-grade product and necessary inventory to support commercial launch;
- the costs associated with payment of milestones and royalties under existing contractual arrangements and/or in-licensing additional products candidates to augment our current pipeline; and
- the timing, receipt and amount of sales of, or milestone payments related to or royalties on, our current or future product candidates, if any.

Until such time, if ever, that we can generate product revenue sufficient to achieve profitability, we expect to finance our cash needs through a combination of public and private equity offerings, debt financings, other third-party funding, strategic alliances, licensing arrangements or marketing and distribution arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing shareholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing shareholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through other third-party funding, strategic alliances, licensing arrangements or marketing and distribution arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we will be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

**Contractual Obligations and Commitments**

The following table summarizes our contractual obligations as of December 31, 2018 and the effects that such obligations are expected to have on our liquidity and cash flows in future periods:

| | Payments Due by Period | | | | |
|---|---|---|---|---|---|
| | Total | Less than 1 Year | 1 to 3 Years | 4 to 5 Years | More than 5 Years |
| | (in thousands) | | | | |
| Research commitments[1] | $ 16,949 | $ 16,604 | $ 345 | $ — | $ — |
| Total | $ 16,949 | $ 16,604 | $ 345 | $ — | $ — |

(1) Amounts in the table reflect commitments for costs associated with external CROs and CMOs engaged to conduct clinical development activities and clinical trials as well as to manufacture clinical trial materials.

Clinical development commitments in the preceding table include agreements that are enforceable and legally binding on us and that specify all significant terms, including fixed or minimum quantities to be purchased; fixed, minimum or variable price provisions; and the approximate timing of the transaction. For obligations with cancellation provisions, the amounts included in the preceding table are limited to the non-cancelable portion of the agreement terms or the minimum cancellation fee.

Under various agreements with third-party licensors and collaborators, we have agreed to make milestone payments and pay royalties and annual maintenance fees to third parties and to meet due diligence requirements based upon specified milestones. We have not included any contingent payment obligations, such as milestones, royalties, or due diligence, in the table above as the amount, timing and likelihood of such payments are not known. We have not included any of the annual maintenance fee payments in the above table, as although the amount and timing are known, we cannot currently determine the final termination dates of the agreements and, as a result, we cannot determine the total amounts of such payments we will be required to make under the agreements. We do not anticipate making material payments related to these arrangements in the next 12 months.

Pursuant to our Funding Agreement with RPI entered in June 2018, we have a commitment to make revenue participation payments to RPI on future global net sales of rimegepant or BHV-3500.

Under the 2018 AstraZeneca Agreement, we are obligated to pay milestone payments to AstraZeneca totaling up to $55.0 million upon the achievement of specified regulatory and commercial milestones and up to $50.0 million upon the achievement of specified sales-based milestones. In addition, we will pay AstraZeneca tiered royalties ranging from high single-digit to low double-digits based on net sales of specified approved products, subject to specified reductions.

Under our license agreement with BMS, we are obligated to make additional development milestone payments of up to $122.5 million for rimegepant or a derivative thereof and up to $74.5 million for other covered product candidates, as well as up to $150.0 million in commercial milestone payments for each licensed product and tiered royalties based on net sales of licensed products under the agreement at percentages in the low to mid-teens.

Under our license agreement with AstraZeneca, we are obligated to make development milestone payments of up to $30.0 million with respect to Rett syndrome and up to $60.0 million for any other indication, as well as commercial milestone payments of up to $120.0 million for all products licensed under the agreement and tiered royalties based on net sales of licensed products under the agreement at mid-single-digit to low double-digit percentages.

Under our license agreement with Yale, we are obligated to make regulatory milestone payments of up to $2.0 million, as well as royalties based on net sales of products from the licensed patents at a low single-digit percentage, subject to a minimum amount of up to $1.0 million per year.

Under our license agreement with Catalent U.K. Swindon Zydis Limited, a subsidiary of Catalent, Inc. ("Catalent") related to BHV-0223, we are obligated to pay up to $1.6 million upon the achievement of specified regulatory and commercial milestones, as well as royalties based on net sales of products licensed under the agreement at a low single-digit percentage. Under our license agreement with Catalent related to rimegepant, we are obligated to pay up to $1.6 million upon the achievement of specified regulatory and commercial milestones.

Under our license agreement with MGH, we are obligated to pay an annual license maintenance fee of up to $0.1 million, to make clinical and regulatory milestone payments of up to $0.8 million and commercial milestone payments of up to $2.5 million, and to pay royalties based on net sales at a low single-digit percentage.

Under our agreement with ALS Biopharma, LLC ("ALS Biopharma") and Fox Chase Chemical Diversity Center, Inc. ("FCCDC") we are obligated to pay $3.0 million upon the achievement of a specified regulatory milestone with respect to the

first licensed product and $1.0 million upon the achievement of a specified regulatory milestone with respect to subsequent products, as well as royalties based on net sales of products licensed under the agreement at a low single-digit percentage.

Under our license agreement with Rutgers, we are obligated to pay an annual license maintenance fee of up to less than $0.01 million per year, to make clinical and regulatory milestone payments of up to $0.8 million, and to pay royalties based on net sales of products at a low single-digit percentage, subject to a minimum amount of up to $100.0 million per year.

Under our commercial consulting agreement with R PHARM US, we are obligated to pay quarterly services fees, as well as milestones of up to $2.5 million based on commercial milestones related to BHV-0223.

**Critical Accounting Policies and Significant Judgments and Estimates**

Our consolidated financial statements are prepared in accordance with generally accepted accounting principles in the United States ("GAAP"). The preparation of our consolidated financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenue, costs and expenses, and the disclosure of contingent assets and liabilities in our financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis.

Our actual results may differ from these estimates under different assumptions or conditions. While our significant accounting policies are described in more detail in the notes to our financial statements appearing at the end of this Annual Report, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our financial statements.

***Accrued Research and Development Expenses***

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advance payments. We make estimates of our accrued expenses as of each balance sheet date in the consolidated financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of these estimates with the service providers and make adjustments if necessary. Examples of estimated accrued research and development expenses include fees paid to:

- vendors, including central laboratories, in connection with preclinical development activities;
- CROs and investigative sites in connection with preclinical and clinical studies; and
- CMOs in connection with drug substance and drug product formulation of preclinical and clinical trial materials.

We base our expenses related to preclinical studies and clinical trials on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple research institutions and CROs that conduct and manage preclinical studies and clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or the amount of prepaid expenses accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

***Non-Cash Share-Based Compensation***

We measure stock options and other share-based awards granted to employees, non-employees, and directors based on the fair value on the date of the grant and recognize the corresponding non-cash compensation expense of those awards over the requisite service period, which is generally the vesting period of the respective award. We have only issued stock options with service-based vesting conditions and record the expense for these awards using the straight-line method.

Prior to the adoption of Accounting Standards Update ("ASU") No. 2018-07, Compensation - Stock Compensation (Topic 718): Improvements to Non-employee Share-based Payment Accounting ("ASU 2018-07"), which is discussed in Note 2 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, for share-based awards granted to consultants and non-employees, we recognized non-cash compensation expense over the period during which services were rendered by such consultants and non-employees until completed. At the end of each financial reporting period prior to completion of the service, the fair value of these awards was remeasured using the then-current fair value of our common shares and updated assumption inputs in the Black-Scholes option-pricing model.

We estimate the fair value of each stock option grant using the Black-Scholes option-pricing model, which uses as inputs the fair value of our common shares and assumptions we make for the volatility of our common shares, the expected term of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options and our expected dividend yield.

***Valuation of Warrant Liability***

In connection with entering into the Credit Agreement, we issued warrants to purchase our common shares to the guarantor and co-guarantor of our obligations under the agreement. On January 26, 2018, the anti-dilution price protection provisions contained within the warrants expired. Due to the expiration of these provisions, we discontinued classification of these warrants as a liability, and have accordingly reclassified them to additional paid-in capital within shareholders' equity. On expiration, the fair value of the warrant liability was determined based on significant inputs not observable in the market, which represents a Level 3 measurement within the fair value hierarchy.

We utilized the Black-Scholes option pricing model to value the warrant liability. The Black-Scholes option pricing model incorporated assumptions and estimates to value the warrant liability. Estimates and assumptions impacting the fair value measurement included the number of shares for which the warrants will be exercisable, the fair value per share of the underlying common shares issuable upon exercise of the warrants, the remaining contractual term of the warrants, the risk-free interest rate, the expected dividend yield, and the expected volatility of the price of the underlying common shares. The fair value per share of the common shares was based on the closing trading price of the shares on January 26, 2018, the day of expiration, and the increase in the fair value of the common shares during the time period from December 31, 2017 to expiration is the primary reason for the increase in the fair value of the warrant liability during the same period. We were a private company prior to the IPO in May 2017 and therefore lacked company-specific historical and implied volatility information of our shares. Therefore, we estimated the expected share volatility based on the historical volatility of publicly traded peer companies for a term equal to the remaining contractual term of the warrants. The risk-free interest rate was determined by reference to the U.S. Treasury yield curve for time periods approximately equal to the remaining contractual term of the warrants. We estimated a 0% expected dividend yield based on the fact that the We have never paid or declared dividends and does not intend to do so in the foreseeable future.

***Equity method investment, including related impairment***

An assessment of whether or not we have the power to direct activities that most significantly impact Kleo's economic performance and to identify the party that obtains the majority of the benefits of the investment was performed as of December 31, 2018 and December 31, 2017, and will be performed as of each subsequent reporting date. After each of these assessments, we concluded that the activities that most significantly impact Kleo's economic performance are the ability to direct its research activities, the ability to select vendors to perform the research, the ability to maintain research staff and the ability to raise additional funds, each of which are directed by Kleo. Based on the outcome of these assessments, we concluded that our investment in Kleo should be accounted for under the equity method. Changes related to this assessment could have a material impact on our financial statements.

We also periodically review the carrying value of our investment in Kleo to determine if there has been an other-than-temporary decline in carrying value. A variety of factors are considered when determining if a decline in carrying value is other than temporary, including, among other factors, Kleo's financial condition and business prospects, as well as our intent with regard to the investment. Changes related to the analysis of impairment of our investment in Kleo could have a material impact on our financial statements.

***Non-Cash Interest Expense on Liability Related to Sale of Future Royalties***

We have accounted for the Funding Agreement with RPI as a liability financing. The debt will be amortized under the effective interest rate method and, accordingly, we are recognizing non-cash interest expense over the estimated term of the Funding Agreement. The liability related to sale of future royalties, and the debt amortization, are based on our current estimate of future royalties expected to be paid over the term of the Funding Agreement. These estimates include projections we make and projections from outside the Company and involve significant judgment and involve inherent uncertainties. We will periodically assess the expected royalty payments and, if materially different than our previous estimate, we will adjust the

liability and prospectively recognize related non-cash interest expense. The transaction costs associated with the liability will be amortized to non-cash interest expense over the estimated term of the Funding Agreement.

**Off-Balance Sheet Arrangements**

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

**Recently Issued Accounting Pronouncements**

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2 to our consolidated financial statements appearing at the end of this Annual Report.

**Item 7A. Quantitative and Qualitative Disclosures about Market Risks**

*Interest Rate Risk*

The market risk inherent in our financial instruments and in our financial position has historically been the potential loss arising from adverse changes in interest rates. In August 2017, we repaid all outstanding amounts under the Credit Agreement and, as a result, we no longer have any exposure to interest rate risk related to indebtedness as of December 31, 2018. As of December 31, 2018 and 2017, we had cash of $264.2 million and $131.5 million, respectively. As of December 31, 2018, we held our cash in non-interest-bearing money market accounts and accordingly, the value of these accounts is not subject to fluctuation in interest rates.

Prior to the completion of our IPO in May 2017, we adopted an investment policy related to the use of the net proceeds from the sale of our common shares in our IPO, pursuant to which we hold such net proceeds in non-interest bearing accounts, with the goal of capital preservation and liquidity so that such funds are readily available to fund our operations.

We do not engage in any hedging activities against changes in interest rates or any other market risks. We do not have any foreign currency or other derivative financial instruments.

**ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA**

The consolidated financial statements and supplementary data of the Company required in this item are set forth beginning on page F-1.

**ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE**

None.

**ITEM 9A. CONTROLS AND PROCEDURES**

***Evaluation of Disclosure Controls and Procedures***

The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), refers to controls and procedures that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that such information is accumulated and communicated to a company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure.

In designing and evaluating our disclosure controls and procedures, management recognizes that disclosure controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the disclosure controls and procedures are met. Additionally, in designing disclosure controls and procedures, our management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible disclosure controls and procedures. The design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, controls may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a control system, misstatements due to error or fraud may occur and not be detected.

Based on the evaluation of our disclosure controls and procedures, our Chief Executive Officer and Chief Financial Officer have concluded that, as of December 31, 2018, our disclosure controls and procedures were effective at the reasonable assurance level.

***Management's Report on Internal Control over Financial Reporting***

Management of the Company is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Management conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2018 based on the framework in *Internal Control-Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). Based on that evaluation, management has concluded that the Company's internal control over financial reporting was effective as of December 31, 2018.

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

***Remediation of Previously-Identified Material Weaknesses in Internal Control over Financial Reporting***

In connection with the preparation of our financial results for the years ended December 31, 2014 and 2015, our management concluded that, as of December 31, 2015, our internal control over financial reporting was not effective as a result of material weaknesses in our control over financial reporting. The material weaknesses remained unremediated as of September 30, 2018 as despite making progress towards the remediation of the material weaknesses, they could not be considered remediated until the applicable remedial controls operate for a sufficient period of time and management has concluded, through testing, that these controls are operating effectively.

A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our financial statements will not be prevented or detected on a timely basis. The material weaknesses previously identified in our internal control over financial reporting included the following:

- We did not design or maintain an effective control environment commensurate with our financial reporting requirements. We lacked a sufficient number of trained professionals with an appropriate level of accounting knowledge, training and experience to appropriately analyze, record and disclose accounting matters timely and accurately. This material weakness contributed to the following material weakness:
    - We did not design and maintain formal accounting policies, procedures and controls to achieve complete, accurate and timely financial accounting, reporting and disclosures, including controls over the preparation and review of account reconciliations and journal entries. Additionally, we did not design and maintain controls over the appropriate classification and presentation of accounts and disclosures in the financial statements.
    - We did not design and maintain formal accounting policies, processes and controls to analyze, account for and disclose complex transactions. Specifically, we did not design and maintain controls to analyze, account for and disclose complex licensing agreements, income taxes, variable interest entities, debt arrangements, equity method investments, share-based compensation arrangements, derivative liabilities, warrants to purchase common shares and contingently issuable equity.
    - We did not design and maintain controls over our supervision and review of the completeness and accuracy of third-party vendors' computations supporting our common share valuations.
- We did not design and maintain controls over the operating effectiveness of information technology, or IT, general controls for information systems that are relevant to the preparation of our financial statements. Specifically, we did not design and maintain effective controls over program change management; user access, including segregation of duties; or computer operations.

In response to the identified material weaknesses, we took a number of actions to improve our internal control over financial reporting during the year ended December 31, 2018, including the following:

- Finalized design and implementation of our financial control environment, including policies and procedures, transaction-level controls, entity-level controls, information technology general controls, and controls over the maintenance of appropriate segregation of duties.
- Implemented controls over journal entries and account reconciliations.
- Implemented controls over the supervision and review of the completeness and accuracy of analyses performed by third-party vendors.
- Hired additional finance staff with significant experience with financial controls and reporting under generally accepted accounting principles.
- Completed the implementation of a new enterprise resource planning system, a new share-based compensation system, and a new external financial reporting software.
- Implemented formal disclosure controls and procedures, including controls over the accounting and disclosure for significant unusual transactions, the formalization of a disclosure committee, and requiring management sub-certifications from employees in key functional areas.
- Engaged a third party firm to support our compliance with Section 404 of the Sarbanes-Oxley Act and finalized a project supporting design and operating effectiveness of our internal controls over financial reporting.

Management concluded that, as a result of the implementation of these actions during the year ended December 31, 2018, and the results of our testing over the design and operating effectiveness of controls, our remediation efforts have been successful and that the previously-identified material weaknesses in our internal controls have been remediated as of December 31, 2018.

***Changes in Internal Controls over Financial Reporting***

There have been no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the three months ended December 31, 2018 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

**ITEM 9B. OTHER INFORMATION**

Not applicable.

## PART III

We will file a definitive Proxy Statement for our 2019 Annual Meeting of Shareholders (the "2019 Proxy Statement") with the SEC, pursuant to Regulation 14A, not later than 120 days after the end of our fiscal year. Accordingly, certain information required by Part III has been omitted under General Instruction G(3) to Form 10-K. Only those sections of the 2019 Proxy Statement that specifically address the items set forth herein are incorporated by reference.

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

The information required by this Item is incorporated herein by reference to the information that will be contained in our 2019 Proxy Statement under the captions "Information Regarding the Board of Directors and Corporate Governance," "Election of Directors," "Executive Officers" and "Section 16(a) Beneficial Ownership Reporting Compliance."

**Item 11. Executive Compensation**

The information required by this Item is incorporated herein by reference to the information that will be contained in the 2019 Proxy Statement under the captions "Executive Compensation" and "Director Compensation."

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

The information required by this Item is incorporated herein by reference to the information that will be contained in the 2019 Proxy Statement under the captions "Security Ownership of Certain Beneficial Owners and Management" and "Securities Authorized for Issuance under Equity Compensation Plans."

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

The information required by this Item is incorporated herein by reference to the information that will be contained in the 2019 Proxy Statement under the captions "Transactions with Related Persons" and "Independence of the Board of Directors."

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

The information required by this Item is incorporated herein by reference to the information that will be contained in the 2019 Proxy Statement under the caption "Ratification of Selection of Independent Auditors."

## PART IV

### Item 15. Exhibits, Financial Statement Schedules

a. The following documents are filed as part of this report:

(1) Financial Statements:

The financial statements required by this item are submitted in a separate section beginning on page F-1 of this report.

(2) Financial Statement Schedules:

All other financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the consolidated financial statements or the notes thereto.

(3) Exhibits.

| Exhibit Number* | Description of Document |
|---|---|
| 2.1 | Securities Purchase Agreement between Kleo Pharmaceuticals, Inc. and the Registrant, dated as of August 29, 2016 (incorporated by reference to Exhibit 2.1 to the Registrant's Current Report on Form 8-K (File No. 001-38080) filed with the Securities and Exchange Commission on June 14, 2017). |
| 2.2 | First Subscription Agreement between Kleo Pharmaceuticals, Inc. and the Registrant, dated as of October 5, 2017 (incorporated by reference to Exhibit 2.2 to the Registrant's Current Report on Form 8-K (File No. 001-38080) filed with the Securities and Exchange Commission on October 12, 2017). |
| 2.3 | Second Subscription Agreement between Kleo Pharmaceuticals, Inc. and the Registrant, dated as of October 5, 2017 (incorporated by reference to Exhibit 2.3 to the Registrant's Current Report on Form 8-K (File No. 001-38080) filed with the Securities and Exchange Commission on October 12, 2017). |
| 3.1 | Memorandum and Articles of Association (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-38080) filed with the Securities and Exchange Commission on May 12, 2017). |
| 4.1 | Investors' Rights Agreement, dated as of October 31, 2016, by and among the Registrant and certain of its shareholders (incorporated by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-217214) filed with the Securities and Exchange Commission on April 7, 2017). |
| 4.2 | Term Note, dated August 30, 2016, issued to Wells Fargo Bank, National Association (incorporated by reference to Exhibit 4.3 to the Registrant's Registration Statement on Form S-1 (File No. 333-217214) filed with the Securities and Exchange Commission on April 7, 2017). |
| 4.3 | Warrant, dated January 26, 2017, issued to John Childs (incorporated by reference to Exhibit 4.4 to the Registrant's Registration Statement on Form S-1 (File No. 333-217214) filed with the Securities and Exchange Commission on April 7, 2017). |
| 4.4 | Warrant, dated January 26, 2017, issued to Gregory Bailey (incorporated by reference to Exhibit 4.5 to the Registrant's Registration Statement on Form S-1 (File No. 333-217214) filed with the Securities and Exchange Commission on April 7, 2017). |

| Exhibit Number* | | Description of Document |
|---|---|---|
| | 4.5 | Warrants, dated August 15, 2015, issued to ALS Biopharma, LLC (incorporated by reference to Exhibit 4.6 to the Registrant's Registration Statement on Form S-1 (File No. 333-217214) filed with the Securities and Exchange Commission on April 7, 2017). |
| | 10.1 # | License Agreement, by and between the registrant and Bristol-Myers Squibb Company, dated as of July 8, 2016 (incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-217214) filed with the Securities and Exchange Commission on April 7, 2017). |
| | 10.2 # | ALS Biopharma Agreement, by and among the registrant, ALS Biopharma, LLC and Fox Chase Chemical Diversity Center Inc., dated as of August 10, 2015, as amended to date (incorporated by reference to Exhibit 10.2 to the Registrant's Amendment No. 1 to Registration Statement on Form S-1 (File No. 333-217214) filed with the Securities and Exchange Commission on April 24, 2017). |
| | 10.3 # | License Agreement, by and between the registrant and AstraZeneca AB, dated as of October 5, 2016 (incorporated by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form S-1 (File No. 333-217214) filed with the Securities and Exchange Commission on April 7, 2017). |
| | 10.4 # | Agreement, by and between the registrant and Yale University, dated as of September 30, 2013, as amended to date (incorporated by reference to Exhibit 10.4 to the Registrant's Amendment No. 1 to Registration Statement on Form S-1 (File No. 333-217214) filed with the Securities and Exchange Commission on April 24, 2017). |
| | 10.5 # | Zydis® Development and License Agreement, by and between the registrant and Catalent U.K. Swindon Zydis Limited, dated as of March 9, 2015 (incorporated by reference to Exhibit 10.5 to the Registrant's Amendment No. 1 to Registration Statement on Form S-1 (File No. 333-217214) filed with the Securities and Exchange Commission on April 24, 2017). |
| | 10.6 # | Exclusive Patent License Agreement, by and between the registrant and The General Hospital Corporation d/b/a Massachusetts General Hospital, dated as of September 13, 2014 (incorporated by reference to Exhibit 10.6 to the Registrant's Amendment No. 1 to Registration Statement on Form S-1 (File No. 333-217214) filed with the Securities and Exchange Commission on April 24, 2017). |
| | 10.7 # | Exclusive License Agreement, by and between the registrant and Rutgers, the State University of New Jersey, dated as of June 15, 2016 (incorporated by reference to Exhibit 10.7 to the Registrant's Amendment No. 1 to Registration Statement on Form S-1 (File No. 333-217214) filed with the Securities and Exchange Commission on April 24, 2017). |
| | 10.8 | Credit Agreement, by and between the registrant and Wells Fargo Bank, National Association, dated as of August 30, 2016 (incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1 (File No. 333-217214) filed with the Securities and Exchange Commission on April 7, 2017). |
| | 10.9 + | 2014 Equity Incentive Plan (incorporated by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S-1 (File No. 333-217214) filed with the Securities and Exchange Commission on April 7, 2017). |

| Exhibit Number* | | Description of Document |
|---|---|---|
| 10.10 | + | Form of Share Option Agreement under 2014 Equity Incentive Plan (incorporated by reference to Exhibit 10.10 to the Registrant's Registration Statement on Form S-1 (File No. 333-217214) filed with the Securities and Exchange Commission on April 7, 2017). |
| 10.11 | + | 2017 Equity Incentive Plan (incorporated by reference to Exhibit 4.4 to the Registrant's Registration Statement on Form S-8 (File No. 333-218193) filed with the Securities and Exchange Commission on May 23, 2017). |
| 10.12 | + | Form of Stock Option Grant Notice and Stock Option Agreement under 2017 Equity Incentive Plan (incorporated by reference to Exhibit 10.12 to the Registrant's Amendment No. 1 to Registration Statement on Form S-1 (File No. 333-217214) filed with the Securities and Exchange Commission on April 24, 2017). |
| 10.13 | + | Form of Restricted Stock Unit Grant Notice and Restricted Stock Unit Award Agreement under 2017 Equity Incentive Plan (incorporated by reference to Exhibit 10.13 to the Registrant's Amendment No. 1 to Registration Statement on Form S-1 (File No. 333-217214) filed with the Securities and Exchange Commission on April 24, 2017). |
| 10.14 | + | 2017 Employee Share Purchase Plan (incorporated by reference to Exhibit 4.7 to the Registrant's Registration Statement on Form S-8 (File No. 333-218193) filed with the Securities and Exchange Commission on May 23, 2017). |
| 10.15 | + | Form of Indemnification Agreement with non-employee directors (incorporated by reference to Exhibit 10.15 to the Registrant's Amendment No. 2 to Registration Statement on Form S-1 (File No. 333-217214) filed with the Securities and Exchange Commission on May 1, 2017). |
| 21.1 | | Subsidiaries of the Registrant. |
| 23.1 | | Consent of PricewaterhouseCoopers LLP. |
| 24.1 | | Power of Attorney (contained on signature page hereto). |
| 31.1 | | Certification of Principal Executive Officer under Section 302 of the Sarbanes-Oxley Act. |
| 31.2 | | Certification of Principal Financial Officer under Section 302 of the Sarbanes-Oxley Act. |
| 32.1 | @ | Certifications of Principal Executive Officer and Principal Financial Officer under Section 906 of the Sarbanes-Oxley Act. |
| 101.SCH | | XBRL Taxonomy Extension Schema Document |
| 101.CAL | | XBRL Taxonomy Extension Calculation Linkbase Document |
| 101.DEF | | XBRL Taxonomy Extension Definition Linkbase Document |
| 101.LAB | | XBRL Taxonomy Extension Label Linkbase Document |
| 101.PRE | | XBRL Taxonomy Extension Presentation Linkbase Document |

* The XBRL instance document does not appear in the interactive data file because its XBRL tags are embedded within the inline XBRL document.

# Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment and have been separately filed with the Securities and Exchange Commission.

+ Indicates management contract or compensatory plan.

@ These certifications are being furnished solely to accompany this Annual Report pursuant to 18 U.S.C. Section 1350, and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and are not to be incorporated by reference into any filing of the Registrant, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

**Item 16. Form 10-K Summary**

Not applicable.

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

BIOHAVEN PHARMACEUTICAL HOLDING COMPANY LTD.

Date: February 28, 2019

By: /s/ VLAD CORIC, M.D.
Vlad Coric, M.D.
*Chief Executive Officer*
*(On behalf of the Registrant and as the Principal Executive Officer)*

By: /s/ JIM ENGELHART
Jim Engelhart
*Chief Financial Officer*
*(Principal Financial Officer)*

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

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

| Signature | Title | Date |
|---|---|---|
| /s/ VLAD CORIC, M.D.<br>Vlad Coric, M.D. | Chief Executive Officer and Director<br>(Principal Executive Officer) | February 28, 2019 |
| /s/ JAMES ENGELHART<br>James Engelhart | Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer) | February 28, 2019 |
| /s/ DECLAN DOOGAN, M.D.<br>Declan Doogan, M.D. | Director | February 28, 2019 |
| /s/ ERIC AGUIAR, M.D.<br>Eric Aguiar, M.D. | Director | February 28, 2019 |
| /s/ GREGORY H. BAILEY, M.D.<br>Gregory H. Bailey, M.D. | Director | February 28, 2019 |
| /s/ ROBERT REPELLA<br>Robert Repella | Director | February 28, 2019 |
| /s/ JOHN W. CHILDS<br>John W. Childs | Director | February 28, 2019 |
| /s/ JULIA P. GREGORY<br>Julia P. Gregory | Director | February 28, 2019 |

**Biohaven Pharmaceutical Holding Company Ltd.**

**Financial Statements**

**For the Years Ended December 31, 2018, 2017 and 2016**

**Report of Independent Registered Public Accounting Firm**

To the Board of Directors and Shareholders of
Biohaven Pharmaceutical Holding Company Ltd.

***Opinions on the Financial Statements and Internal Control over Financial Reporting***

We have audited the accompanying consolidated balance sheets of Biohaven Pharmaceutical Holding Company Ltd. and its subsidiaries (the "Company") as of December 31, 2018 and 2017, and the related consolidated statements of operations and comprehensive loss, of convertible preferred shares and shareholders' equity (deficit), and of cash flows for each of the three years in the period ended December 31, 2018, including the related notes (collectively referred to as the "consolidated financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2018, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the COSO.

***Basis for Opinions***

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Report on Internal Control over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on the Company's consolidated financial statements and on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

***Definition and Limitations of Internal Control over Financial Reporting***

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

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

/s/ PricewaterhouseCoopers LLP
Hartford, Connecticut
February 28, 2019

We have served as the Company's auditor since 2017.

**BIOHAVEN PHARMACEUTICAL HOLDING COMPANY LTD.**
**CONSOLIDATED BALANCE SHEETS**
**(Amounts in thousands, except share and per share amounts)**

| | December 31, | |
|---|---|---|
| | 2018 | 2017 |
| **Assets** | | |
| Current assets: | | |
| Cash | $ 264,249 | $ 131,468 |
| Prepaid expenses and other current assets | 8,090 | 5,197 |
| Total current assets | 272,339 | 136,665 |
| Property and equipment, net (Note 6) | 6,248 | 2,344 |
| Equity method investment (Note 5) | 11,414 | 7,847 |
| Other assets | 11 | 32 |
| Total assets | $ 290,012 | $ 146,888 |
| **Liabilities and Shareholders' Equity** | | |
| Current liabilities: | | |
| Accounts payable | 10,752 | 4,721 |
| Accrued expenses | 8,782 | 4,708 |
| Total current liabilities | 19,534 | 9,429 |
| Non-recourse debt related to sale of future royalties, net (Note 8) | 117,515 | — |
| Warrant liability | — | 4,021 |
| Other long-term liabilities | 2,043 | 1,467 |
| Total liabilities | 139,092 | 14,917 |
| Commitments and contingencies (Note 16) | | |
| Shareholders' equity: | | |
| Common shares, no par value; 200,000,000 shares authorized as of December 31, 2018 and 2017; 44,197,549 and 36,057,748 shares issued and outstanding as of December 31, 2018 and December 31, 2017, respectively | 554,384 | 311,061 |
| Additional paid-in capital | 40,104 | 23,556 |
| Accumulated deficit | (443,568) | (202,646) |
| Total shareholders' equity | 150,920 | 131,971 |
| Total liabilities, convertible preferred shares and shareholders' equity | $ 290,012 | $ 146,888 |

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

**BIOHAVEN PHARMACEUTICAL HOLDING COMPANY LTD.**
**CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS**
**(Amounts in thousands, except share and per share amounts)**

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Operating expenses: | | | |
| Research and development | $ 189,951 | $ 89,441 | $ 55,529 |
| General and administrative | 34,603 | 18,141 | 5,109 |
| Total operating expenses | 224,554 | 107,582 | 60,638 |
| Loss from operations | (224,554) | (107,582) | (60,638) |
| Other income (expense): | | | |
| Interest expense | (38) | (906) | (385) |
| Non-cash interest expense on liability related to sale of future royalties | (11,726) | — | — |
| Change in fair value of warrant liability | (1,182) | (3,241) | 154 |
| Change in fair value of derivative liability | — | 512 | (65) |
| Change in fair value of contingent equity liability | — | (13,082) | (2,263) |
| Loss from equity method investment | (2,808) | (1,885) | (247) |
| Other | (147) | — | — |
| Total other income (expense), net | (15,901) | (18,602) | (2,806) |
| Loss before provision for income taxes | (240,455) | (126,184) | (63,444) |
| Provision for income taxes | 467 | 1,006 | 90 |
| Net loss and comprehensive loss | (240,922) | (127,190) | (63,534) |
| Net loss attributable to non-controlling interests | — | — | 143 |
| Accretion of beneficial conversion feature on Series A preferred shares | — | (12,006) | — |
| Net loss attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd. | $ (240,922) | $ (139,196) | $ (63,677) |
| Net loss per share attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd.—basic and diluted | $ (6.15) | $ (5.00) | $ (5.05) |
| Weighted average common shares outstanding—basic and diluted | 39,188,458 | 27,845,576 | 12,608,366 |

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

**BIOHAVEN PHARMACEUTICAL HOLDING COMPANY LTD.**
**CONSOLIDATED STATEMENT OF CONVERTIBLE PREFERRED SHARES AND SHAREHOLDERS' EQUITY (DEFICIT)**
**(Amounts in thousands, except share and per share amounts)**

| | Series A Convertible Preferred Shares | | Common Shares | | | | Total Biohaven Pharmaceutical Holding Company Ltd. Shareholders' Equity (Deficit) | | |
|---|---|---|---|---|---|---|---|---|---|
| | Shares | Amount | Shares | Amount | Additional Paid-in Capital | Accumulated Deficit | | Non-Controlling Interests | Total Shareholders' Equity (Deficit) |
| **Balances as of December 31, 2015** | — | $ — | 11,569,000 | $ 8,665 | $ 4,258 | $ (11,779) | $ 1,144 | $ (57) | $ 1,087 |
| Issuance of common shares, net of offering costs of $120 | — | — | 1,519,500 | 11,279 | — | — | 11,279 | — | 11,279 |
| Issuance of common share warrant in connection with license agreement (Note 13) | — | — | — | — | 2,127 | — | 2,127 | — | 2,127 |
| Issuance of Series A convertible preferred shares, net of cash offering costs of $1,730 | 4,305,209 | 38,270 | — | — | — | — | — | — | — |
| Issuance of Series A convertible preferred shares as payment of related offering costs | 105,010 | — | — | — | — | — | — | — | — |
| Issuance of Series A convertible preferred shares in settlement of contingent equity liability (Note 13) | 538,150 | 5,000 | — | — | — | — | — | — | — |
| Acquisition of BPI (Note 18) | — | — | — | — | (509) | — | (509) | (86) | (595) |
| Non-cash share-based compensation expense | — | — | — | — | 4,603 | — | 4,603 | — | 4,603 |
| Net loss | — | — | — | — | — | (63,677) | (63,677) | 143 | (63,534) |
| **Balances as of December 31, 2016** | 4,948,369 | 43,270 | 13,088,500 | 19,944 | 10,479 | (75,456) | (45,033) | — | (45,033) |
| Issuance of Series A convertible preferred shares, net of offering costs of $1,334 | 4,305,182 | 38,666 | — | — | — | — | — | — | — |
| Issuance of Series A convertible preferred shares as payment of offering costs | 105,009 | — | — | — | — | — | — | — | — |
| Beneficial conversion feature on Series A convertible preferred shares | — | (12,006) | — | — | 12,006 | — | 12,006 | — | 12,006 |
| Accretion of beneficial conversion feature on Series A convertible preferred shares | — | 12,006 | — | — | (12,006) | — | (12,006) | — | (12,006) |
| Issuance of common shares as payment for equity investment (Note 5) | — | — | 32,500 | 352 | — | — | 352 | — | 352 |
| Conversion of Series A convertible preferred shares to common shares | (9,358,560) | (81,936) | 9,358,560 | 81,936 | — | — | 81,936 | — | 81,936 |
| Issuance of common shares in settlement of contingent equity liability | — | — | 1,883,523 | 32,020 | — | — | 32,020 | — | 32,020 |
| Issuance of common shares upon completion of initial public offering, net of offering costs | — | — | 11,385,000 | 176,128 | — | — | 176,128 | — | 176,128 |
| Issuance of common share warrant as consideration for services | — | — | — | — | 93 | — | 93 | — | 93 |
| Exercise of stock options | — | — | 309,665 | 681 | (255) | — | 426 | — | 426 |
| Non-cash share-based compensation expense | — | — | — | — | 13,239 | — | 13,239 | — | 13,239 |
| Net loss | — | — | — | — | — | (127,190) | (127,190) | — | (127,190) |
| **Balances as of December 31, 2017** | — | — | 36,057,748 | 311,061 | 23,556 | (202,646) | 131,971 | — | 131,971 |
| Issuance of common shares as payment for license agreement | — | — | 109,523 | 4,080 | — | — | 4,080 | — | 4,080 |
| Issuance of common shares upon completion of equity offerings, net of offering costs | — | — | 6,970,171 | 230,339 | — | — | 230,339 | — | 230,339 |
| Exercise of ALS Biopharma warrants, net settlement of shares | — | — | 489,359 | — | — | — | — | — | — |
| Reclassification of warrant liability to equity | — | — | — | — | 5,203 | — | 5,203 | — | 5,203 |
| Exercise of stock options | — | — | 570,748 | 8,904 | (5,580) | — | 3,324 | — | 3,324 |
| Non-cash share-based compensation expense | — | — | — | — | 16,925 | — | 16,925 | — | 16,925 |
| Net loss | — | — | — | — | — | (240,922) | (240,922) | — | (240,922) |
| **Balances as of December 31, 2018** | — | $ — | 44,197,549 | $ 554,384 | $ 40,104 | $ (443,568) | $ 150,920 | $ — | $ 150,920 |

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

**BIOHAVEN PHARMACEUTICAL HOLDING COMPANY LTD.**
**CONSOLIDATED STATEMENTS OF CASH FLOWS**
**(Amounts in thousands, except share and per share amounts)**

| | Year ended December 31, | | |
|---|---|---|---|
| | **2018** | **2017** | **2016** |
| **Cash flows from operating activities:** | | | |
| Net loss | $ (240,922) | $ (127,190) | $ (63,534) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | | |
| Non-cash share-based compensation expense | 16,925 | 13,239 | 4,603 |
| Non-cash interest expense on non-recourse debt related to sale of future royalties | 11,726 | — | — |
| Issuance of common shares as payment for license agreement | 4,080 | — | — |
| Non-cash interest expense | — | 784 | 374 |
| Fair value of contingent equity liability under license agreements | — | — | 21,675 |
| Fair value of warrants issued as consideration for license agreement | — | — | 2,127 |
| Change in fair value of warrant liability | 1,182 | 3,241 | (154) |
| Change in fair value of derivative liability | — | (512) | 65 |
| Change in fair value of contingent equity liability | — | 13,082 | 2,263 |
| Loss from equity method investment | 2,808 | 1,885 | 247 |
| Deferred tax assets | — | 9 | — |
| Other non-cash items | 269 | 64 | (4) |
| Changes in operating assets and liabilities: | | | |
| Prepaid expenses and other current assets | (2,893) | (4,730) | 24 |
| Other assets | 21 | (32) | — |
| Accounts payable | 5,390 | 3,975 | 678 |
| Accrued expenses | 3,697 | 1,341 | 2,148 |
| Other long-term liabilities | 576 | 29 | (16) |
| Net cash used in operating activities | (197,141) | (94,815) | (29,504) |
| **Cash flows from investing activities:** | | | |
| Purchases of property and equipment | (4,165) | (541) | (26) |
| Purchase of equity method investment | (6,375) | (6,627) | (3,000) |
| Net cash used in investing activities | (10,540) | (7,168) | (3,026) |
| **Cash flows from financing activities:** | | | |
| Proceeds from issuance of common shares | 190,125 | 179,996 | 11,399 |
| Proceeds from sale of future royalties | 106,047 | — | — |
| Proceeds from issuance of common stock related to sale of future royalties | 43,953 | — | — |
| Proceeds from issuance of Series A preferred shares | — | 40,000 | 40,000 |
| Proceeds from borrowings | — | — | 5,000 |
| Proceeds from exercise of stock options | 3,324 | 426 | — |
| Payments of related party notes payable | — | (595) | — |
| Repayment of notes payable | | (5,000) | |
| Payments of offering costs | (2,987) | (5,068) | (1,507) |
| Payments of debt issuance costs | — | — | (197) |
| Advanced payment for the second closing of Series A preferred stock | — | — | 67 |
| Net cash provided by financing activities | 340,462 | 209,759 | 54,762 |
| **Net increase in cash** | 132,781 | 107,776 | 22,232 |
| Cash at beginning of period | 131,468 | 23,692 | 1,460 |
| Cash at end of period | $ 264,249 | $ 131,468 | $ 23,692 |
| **Supplemental disclosure of cash flow information:** | | | |
| Cash paid for interest | $ — | $ 122 | $ 11 |
| Cash paid for income taxes | $ 333 | $ 1,049 | $ — |
| **Supplemental disclosure of non-cash investing and financing activities:** | | | |
| Deferred offering costs included in accrued expenses | $ 1,018 | $ — | $ 134 |
| Series A convertible preferred share offering costs included in accrued expenses | $ — | $ — | $ 343 |
| Issuance of warrants to guarantor and co-guarantor of notes payable | $ — | $ — | $ 934 |
| Beneficial conversion feature on Series A preferred shares | $ — | $ 12,006 | $ — |
| Accretion of beneficial conversion feature on Series A preferred shares | $ — | $ 12,006 | $ — |
| Issuance of Series A preferred shares as payment of offering costs | $ — | $ 1,242 | $ 975 |
| Issuance of Series A preferred shares in settlement of contingent equity liability | $ — | $ — | $ 5,000 |
| Issuance of common shares as payment of equity investment | $ — | $ 352 | $ — |
| Issuance of notes payable to related parties in connection with acquisition of BPI | $ — | $ — | $ 595 |
| Purchases of property and equipment under financing lease | $ — | $ 1,787 | $ — |

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

**BIOHAVEN PHARMACEUTICAL HOLDING COMPANY LTD.**
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**
**(Amounts in thousands, except share and per share amounts)**

**1. Nature of the Business and Basis of Presentation**

Biohaven Pharmaceutical Holding Company Ltd. (“we,” “us” or the “Company”) was incorporated in Tortola, British Virgin Islands in September 2013. We are a clinical-stage biopharmaceutical company with a portfolio of innovative, late-stage product candidates targeting neurological diseases, including rare disorders. Our product candidates are based on multiple mechanisms —calcitonin gene-related peptide (“CGRP”) receptor antagonists, glutamate modulators and myeloperoxidase ("MPO") inhibitor—which we believe have the potential to significantly alter existing treatment approaches across a diverse set of neurological indications with high unmet need in both large and orphan indications. The most advanced product candidate from the Company’s CGRP receptor antagonist platform is rimegepant, which the Company is developing for the acute and preventive treatment of migraine and for which it has completed three Phase 3 clinical trials in acute treatment of migraine.

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including, but not limited to, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to secure additional capital to fund operations. Product candidates currently under development will require significant additional research and development efforts, including preclinical and clinical testing and regulatory approval, prior to commercialization. These efforts may require additional capital, additional personnel and infrastructure, and further regulatory and other capabilities. Even if the Company’s product development efforts are successful, it is uncertain when, if ever, the Company will realize revenue from product sales.

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (“GAAP”) and include the accounts of the Company and its subsidiaries after elimination of all intercompany accounts and transactions. Investments in companies in which the Company owns less than a 50% equity interest and where it has the ability to exercise significant influence over the operating and financial policies of the investee are accounted for using the equity method of accounting.

***Biohaven Pharmaceuticals, Inc.***

The Company has historically outsourced all of the research and clinical development for its programs under a master services agreement (the "MSA") with Biohaven Pharmaceuticals, Inc. ("BPI"). BPI was incorporated in the state of Delaware in July 2013. The three founders of BPI, each of whom owned 33.33% of the equity of BPI through December 31, 2016, are related parties of the Company (see Note 18). Substantially all of the operations of BPI have been performed in service to the Company under the terms of the MSA, and substantially all of the revenue for the operations of BPI was provided by us.

From inception, the Company has consolidated the results of BPI. On December 31, 2016, the Company acquired 100% of the issued and outstanding shares of BPI (see Note 18).

From inception through the acquisition of BPI, 100% of the equity in BPI was reflected as a net loss attributable to non-controlling interest on the consolidated statement of operations and comprehensive loss. Since the acquisition of BPI on December 31, 2016, the Company no longer reports any non-controlling interest related to BPI.

***Stock Split***

In October 2016, the Company effected a 500-for-one stock split of its issued and outstanding common shares. Accordingly, all share and per share amounts for all periods presented in the accompanying consolidated financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect this stock split.

***Initial Public Offering***

On May 3, 2017, the Company's registration statement on Form S-1 relating to its initial public offering of its common shares (the "IPO") was declared effective by the Securities and Exchange Commission ("SEC"). The IPO closed on May 9, 2017 and the Company issued and sold 9,900,000 common shares at a public offering price of $17.00 per share for net proceeds of $152,651 after deducting underwriting discounts and commissions of $11,781 and other offering expenses of approximately $3,868. Upon the closing of the IPO, all convertible preferred shares then outstanding converted into an aggregate of 9,358,560 common shares. In addition, on May 9, 2017, the underwriters of the IPO fully exercised their option to purchase additional shares, and on May 11, 2017, the Company issued and sold 1,485,000 common shares for net proceeds of $23,478 after

**1. Nature of the Business and Basis of Presentation (Continued)**

deducting underwriting discounts and commissions of $1,767. Thus, the aggregate net proceeds to the Company from the IPO, after deducting underwriting discounts and commissions and other offering costs, were $176,128.

In connection with the completion of its IPO, the Company issued an aggregate of 1,883,523 common shares to Bristol Myers-Squibb Company ("BMS") and AstraZeneca AB ("AstraZeneca") in satisfaction of obligations to contingently issue equity securities pursuant to the license agreements (see Note 13) for no additional consideration.

Also in connection with the completion of its IPO in May 2017, the Company amended its memorandum and articles of association to authorize the issuance of up to 200,000,000 no par value common shares and 10,000,000 no par value undesignated preferred shares.

***Going Concern***

In accordance with Accounting Standards Update ("ASU") 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Subtopic 205-40)*, the Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the consolidated financial statements are issued.

In June 2018, the Company entered into a funding agreement (the "Funding Agreement") to sell tiered, sales-based royalty rights on global net sales of pharmaceutical products containing the compounds rimegepant or BHV-3500 and certain derivative compounds thereof ("Products") to RPI Finance Trust ("RPI") in exchange for $100,000 in cash (see Note 8). Also in June 2018, in connection with the Funding Agreement, the Company entered into a common stock purchase agreement ("Purchase Agreement") with RPI, pursuant to which the Company, in a private placement, issued and sold 1,111,111 common shares of the Company to RPI. RPI paid the Company $45.00 per share for gross proceeds of $50,000,000 (see Note 11). The aggregate net proceeds to the Company from the transactions with RPI, after deducting issuance costs of $377, was $149,623.

In December 2018, we closed on an underwritten public offering of 3,859,060 of common shares, including the full exercise of the underwriters' option to purchase additional shares, at a price to the public of $37.25 per share. The aggregate net proceeds to us from the offering, after deducting the underwriting discounts and commissions and offering expenses payable, were approximately $134,485.

Through December 31, 2018, the Company has funded its operations primarily with proceeds from sales of preferred and common shares and proceeds from the IPO. The Company has incurred recurring losses since its inception, including net losses of $240,922, $127,190 and $63,534 during the years ended December 31, 2018, 2017 and 2016, respectively. In addition, as of December 31, 2018, the Company had an accumulated deficit of $443,568. The Company expects to continue to generate operating losses for the foreseeable future. As of February 28, 2019, the issuance date of these consolidated financial statements, the Company expects that its cash of $264,249 as of December 31, 2018 will be sufficient to fund operating expenses, financial commitments and other cash requirements through at least one year after the issuance date of these financial statements. The future viability of the Company beyond that point is dependent on its ability to raise additional capital to finance its operations.

To execute its business plans, the Company will require funding to support its continuing operations and pursue its growth strategy. Until such time as the Company can generate significant revenue from product sales, if ever, it expects to finance its operations through the sale of public or private equity, debt financings or other capital sources, including collaborations with other companies or other strategic transactions. The Company may not be able to obtain financing on acceptable terms, or at all. The terms of any financing may adversely affect the holdings or the rights of the Company's shareholders. If the Company is unable to obtain funding, the Company could be forced to delay, reduce or eliminate some or all of its research and development programs, product portfolio expansion or commercialization efforts, which could adversely affect its business prospects.

If the Company is unable to obtain funding, the Company could be forced to delay, reduce or eliminate some or all of its research and development programs, product portfolio expansion or commercialization efforts, which could adversely affect its business prospects, or the Company may be unable to continue operations. Although management continues to pursue these plans, there is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all.

**(Amounts in thousands, except share and per share amounts)**

**2. Summary of Significant Accounting Policies**

***Use of Estimates***

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of income and expenses during the reporting periods. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, the accrual for research and development expenses and the valuation of common shares, stock options, warrants, derivative instruments, contingent equity instruments, and non-cash interest expense on liability related to sale of future royalties. In addition, management's assessment of the Company's ability to continue as a going concern involves the estimation of the amount and timing of future cash inflows and outflows. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. Changes in estimates are recorded in the period in which they become known. Actual results could differ from those estimates.

***Equity Method Investments, Including Related Impairment***

Investments in non-public companies in which the Company owns less than a 50% equity interest and where it has the ability to exercise significant influence over the operating and financial policies of the investee are accounted for using the equity method of accounting. The Company's proportionate share of the net income or loss of the equity method investment is included in other income (expense), net in the consolidated statement of operations and comprehensive loss and results in a corresponding adjustment to the carrying value of the investment on the consolidated balance sheet. Dividends received reduce the carrying value of the investment.

An assessment of whether or not we have the power to direct activities that most significantly impact Kleo's economic performance and to identify the party that obtains the majority of the benefits of the investment was performed as of December 31, 2018 and December 31, 2017, and will be performed as of each subsequent reporting date. After each of these assessments, we concluded that the activities that most significantly impact Kleo's economic performance are the ability to direct its research activities, the ability to select vendors to perform the research, the ability to maintain research staff and the ability to raise additional funds, each of which are directed by Kleo. Based on the outcome of these assessments, we concluded that our investment in Kleo should be accounted for under the equity method. Changes related to this assessment could have a material impact on our financial statements.

We also periodically review the carrying value of our investment in Kleo to determine if there has been an other-than-temporary decline in carrying value. A variety of factors are considered when determining if a decline in carrying value is other than temporary, including, among other factors, Kleo's financial condition and business prospects, as well as our intent with regard to the investment. Changes related to the analysis of impairment of our investment in Kleo could have a material impact on our financial statements.

***Property and Equipment***

Property and equipment are recorded at cost and depreciated or amortized using the straight-line method over the estimated useful lives of the respective assets. As of December 31, 2018, the Company's property and equipment consisted of an office building, office equipment and computer equipment. As of December 31, 2017, the Company's property and equipment consisted of office equipment and computer equipment, as well as construction in progress comprised of computer software and leasehold improvements.

The fixed assets have the following useful lives:

| | |
|---|---|
| Building | 30 years |
| Office equipment | 3 - 5 years |
| Computer software | 3 - 5 years |
| Computer equipment | 3 years |

Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is included in loss from operations. Expenditures for repairs and maintenance are

**2. Summary of Significant Accounting Policies (Continued)**

charged to expense as incurred. Property and equipment are monitored regularly for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable.

***Fair Value Measurements***

Certain assets of the Company are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3—Unobservable inputs that are supported by little or no market activity that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

The Company's warrant liability, derivative liability and contingent equity liability are carried at fair value, based upon Level 3 inputs described above (see Note 3). The carrying values of other current assets, accounts payable and accrued expenses approximate their fair values due to the short-term nature of these assets and liabilities.

***Segment Information***

The Company manages its operations as a single segment, the development of therapies targeting neurological diseases, for the purposes of assessing performance and making operating decisions. All of the Company's tangible assets are held in the United States.

***Research and Development Costs***

Research and development costs are expensed as incurred. Research and development expenses consist of costs incurred in performing research and development activities, including salaries, non-cash share-based compensation and benefits, third-party license fees, and external costs of vendors engaged to conduct clinical development activities and clinical trials as well as to manufacture clinical trial materials. Non-refundable prepayments for goods or services that will be used or rendered for future research and development activities are deferred and capitalized. Such amounts are recognized as an expense as the goods are delivered or the related services are performed, or until it is no longer expected that the goods will be delivered or the services rendered.

The Company has entered into various research and development-related contracts. These agreements are cancelable, and related payments are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the studies or clinical trials, including the phase or completion of events, invoices received and contracted costs. Certain judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical accrual estimates have not been materially different from the actual costs.

***Non-Cash Interest Expense on Liability Related to Sale of Future Royalties***

The Company accounted for the Funding Agreement with RPI as a liability financing, primarily because it has significant continuing involvement in generating the future revenue on which the royalties are based. The debt will be amortized under the effective interest rate method and, accordingly, the Company is recognizing non-cash interest expense over the estimated term of the Funding Agreement. The liability related to sale of future royalties, and the debt amortization, are based on the Company's current estimate of future royalties expected to be paid over the estimated term of the Funding Agreement. The Company will periodically assess the expected royalty payments and, if materially different than its previous estimate, will

**2. Summary of Significant Accounting Policies (Continued)**

prospectively adjust and recognize the related non-cash interest expense. The transaction costs associated with the liability will be amortized to non-cash interest expense over the estimated term of the Funding Agreement.

***Non-Cash Share-Based Compensation***

The Company measures stock options granted to employees, non-employees, and directors based on the fair value on the date of the grant and recognizes non-cash compensation expense of those awards, over the requisite service period, which is generally the vesting period of the respective award. Forfeitures are accounted for as they occur. Generally, the Company issues stock options with only service-based vesting conditions and records the expense for these awards using the straight-line method. The Company also issues, from time to time, stock options with performance-based vesting conditions and records the expense for these awards when the Company concludes that it is probable that the performance condition will be achieved.

Effective July 1, 2018, the Company adopted Accounting Standards Update ("ASU") No. 2018-07, Compensation - Stock Compensation (Topic 718): Improvements to Non-employee Share-based Payment Accounting ("ASU 2018-07"), which sets out to simplify the accounting for non-employee share-based awards. The ASU expands the scope of Topic 718, Compensation-Stock Compensation, which currently only includes share-based payments issued to employees, to also include share-based payments issued to non-employees for goods and services. Consequently, the accounting for share-based payments to non-employees and employees is substantially aligned. ASU 2018-07 impacts the value at which share-based payments to non-employees is recognized.

Prior to the adoption of ASU 2018-07 for share-based awards granted to non-employees, including consultants, non-cash compensation expense was recognized over the period during which services were rendered by such non-employees until completed. At the end of each financial reporting period prior to completion of the service, the fair value of the unvested awards were remeasured using the then-current fair value of the Company's common shares and updated assumption inputs in the Black-Scholes option-pricing model.

After adoption of ASU 2018-07, the measurement date for non-employee awards is the date of the grant. The non-cash compensation expense for non-employees is recognized, without changes in the fair value of the award, over the requisite service period, which is the vesting period of the respective award. The non-cash compensation expense for non-employees was measured as of the adoption date of July 1, 2018, and this amount is the basis for prospective expense recognition. All of the Company's non-employee awards were previously measured as of June 30, 2018. Accordingly, no cumulative adjustment to beginning retained earnings was recorded as a result of the ASU 2018-07 adoption, as the measured value prior to adoption and the remeasured value on the date of adoption were materially the same.

The Company classifies non-cash share-based compensation expense in its consolidated statement of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model. The Company lacks a sufficient history of company-specific historical and implied volatility information for its shares. Therefore, it estimates its expected share price volatility based on the historical volatility of publicly traded peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded share price. The expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The expected term of stock options granted to non-employees is equal to the contractual term of the option award. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends on common shares and does not expect to pay any cash dividends in the foreseeable future.

***Warrant Liability***

In connection with entering into a credit agreement, the Company issued warrants to purchase common shares to two of the Company's directors in connection with a guarantee of its obligations under the agreement (see Note 9). The Company classifies the warrants as a liability on its consolidated balance sheet because each warrant represents a freestanding financial instrument that is not indexed to the Company's own shares. The warrant liability was initially recorded at fair value upon entering into the credit agreement and is subsequently remeasured to fair value at each reporting date. Changes in the fair value of the warrant liability are recognized as a component of other income (expense), net in the consolidated statement of operations and comprehensive loss. Changes in the fair value of the warrant liability will continue to be recognized until the

**2. Summary of Significant Accounting Policies (Continued)**

warrants are exercised, expire or qualify for equity classification. Changes in the fair value of the warrant liability, until expiration of the anti-dilution price protection provisions, are recognized as a component of other income (expense), net, in the Company's consolidated statement of operations and comprehensive loss. Upon expiration of the provision, the Company discontinued classification of these warrants as a liability, and has accordingly reclassified the fair value to additional paid-in capital within shareholders' equity.

***Income Taxes***

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the consolidated financial statements or in the Company's tax returns. Deferred tax assets and liabilities are determined on the basis of the differences between the consolidated financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies. The provision for income taxes includes the effects of applicable tax reserves, or unrecognized tax benefits, as well as the related net interest and penalties.

***Net Income (Loss) per Share***

The Company follows the two-class method when computing net income (loss) per share as the Company has issued shares that meet the definition of participating securities. The two-class method determines net income (loss) per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income available to common shareholders for the period to be allocated between common and participating securities based upon their respective rights to receive dividends as if all income for the period had been distributed. Net income (loss) per share attributable to common shareholders is calculated based on net income (loss) attributable to Biohaven Pharmaceutical Holding Company Ltd. and excludes net income (loss) attributable to non-controlling interests for relevant periods.

Basic net income (loss) per share attributable to common shareholders is computed by dividing the net income (loss) attributable to common shareholders by the weighted average number of common shares outstanding for the period. Diluted net income (loss) attributable to common shareholders is computed by adjusting net income (loss) attributable to common shareholders to reallocate undistributed earnings based on the potential impact of dilutive securities. Diluted net income (loss) per share attributable to common shareholders is computed by dividing the diluted net income (loss) attributable to common shareholders by the weighted average number of common shares outstanding for the period, including potential dilutive common shares. For purpose of this calculation, outstanding options, warrants to purchase common shares, convertible preferred shares and contingently issuable equity are considered potential dilutive common shares.

The Company's convertible preferred shares contractually entitled the holders of such shares to participate in dividends but contractually did not require the holders of such shares to participate in losses of the Company. In periods in which the Company reports a net loss attributable to common shareholders, diluted net loss per share attributable to common shareholders is the same as basic net loss per share attributable to common shareholders, since potentially dilutive common shares are considered to be anti-dilutive.

***Recently Adopted Accounting Pronouncements***

Effective January 1, 2018, the Company adopted ASU No. 2017-09, Compensation—Stock Compensation (Topic 718): Scope of Modification Accounting ("ASU 2017-09"), which clarifies when to account for a change to the terms or conditions of a share-based payment award as a modification. Under the new guidance, modification accounting is required only if the fair value, the vesting conditions, or the classification of the award (as equity or liability) changes as a result of the change in terms or conditions. The adoption of this new guidance had no impact on the Company's financial position or operating results.

Effective January 1, 2018, the Company adopted ASU 2016-18, "Statement of Cash Flows (Topic 230): Restricted Cash," which requires entities to show the change in the total of cash, cash equivalents, restricted cash and restricted cash equivalents within the statement of cash flows. The guidance is effective retrospectively. As a result, the Company retrospectively included

**2. Summary of Significant Accounting Policies (Continued)**

restricted cash in the beginning cash for the twelve months ended December 31, 2017 on the consolidated statement of cash flows, and no longer separately presents transfers between unrestricted cash and restricted cash. The Company did not have restricted cash as of December 31, 2018 or December 31, 2017.

Effective January 1, 2018, the Company adopted ASU No. 2016-15, Statement of Cash Flows: Classification of Certain Cash Receipts and Cash Payments ("ASU 2016-15"), which addresses diversity in practice in how certain cash receipts and cash payments are presented and classified in the statement of cash flows. The adoption of this new guidance had no impact on the Company's financial position or operating results.

Effective July 1, 2018, the Company adopted Accounting Standards Update ("ASU") No. 2018-07, Compensation - Stock Compensation (Topic 718): Improvements to Non-employee Share-based Payment Accounting ("ASU 2018-07"), which sets out to simplify the accounting for non-employee share-based awards. The ASU expands the scope of Topic 718, Compensation-Stock Compensation, which currently only includes share-based payments issued to employees, to also include share-based payments issued to non-employees for goods and services. Consequently, the accounting for share-based payments to non-employees and employees is substantially aligned. ASU 2018-07 impacts the value at which share-based payments to non-employees is recognized.

Prior to the adoption of ASU 2018-07 for share-based awards granted to non-employees, including consultants, non-cash compensation expense was recognized over the period during which services were rendered by such non-employees until completed. At the end of each financial reporting period prior to completion of the service, the fair value of the unvested awards were remeasured using the then-current fair value of the Company's common shares and updated assumption inputs in the Black-Scholes option-pricing model.

After adoption of ASU 2018-07, the measurement date for non-employee awards is the date of the grant. The non-cash compensation expense for non-employees is recognized, without changes in the fair value of the award, over the requisite service period, which is the vesting period of the respective award. The non-cash compensation expense for non-employees was measured as of the adoption date of July 1, 2018, and this amount is the basis for prospective expense recognition. All of the Company's non-employee awards were previously measured as of June 30, 2018. Accordingly, no cumulative adjustment to beginning retained earnings was recorded as a result of the ASU 2018-07 adoption, as the measured value prior to adoption and the remeasured value on the date of adoption were materially the same.

***Recently Issued Accounting Pronouncements***

In February 2016, the FASB issued ASU No. 2016-02, Leases (Topic 842) ("ASU 2016-02"), which sets out the principles for the recognition, measurement, presentation and disclosure of leases for both parties to a contract (i.e., lessees and lessors). The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease, respectively. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less will be accounted for similar to existing guidance for operating leases today. ASU 2016-02 (Accounting Standards Codification ("ASC") Topic 842) supersedes the previous leases standard, ASC 840, Leases. The standard is effective for public entities for annual periods beginning after December 15, 2018 and for interim periods within those fiscal years. Subsequently, in July of 2018, the FASB issued ASU No. 2018-10, Codification Improvements to Topic 842, Leases ("ASU 2018-10"), and ASU No. 2018-11, Leases (Topic 842): Targeted Improvements ("ASU 2018-11"), both of which clarify and enhance the certain amendments made in ASU 2016-02 and will be adopted in conjunction with ASU 2016-02. The Company intends to elect the package of practical expedients and is currently evaluating the impact that the adoption of ASU 2016-02 will have on its consolidated financial statements.

(Amounts in thousands, except share and per share amounts)

**3. Fair Value of Financial Assets and Liabilities**

The following table presents information about the Company's financial assets and liabilities measured at fair value on a recurring basis and indicate the level of the fair value hierarchy utilized to determine such fair values:

| | Fair Value Measurement as of December 31, 2017 Using: | | | |
|---|---|---|---|---|
| | Level 1 | Level 2 | Level 3 | Total |
| Liabilities: | | | | |
| Warrant liability | $ — | $ — | $ 4,021 | $ 4,021 |
| | $ — | $ — | $ 4,021 | $ 4,021 |

The Company held no financial assets or liabilities measured at fair value on a recurring basis as of December 31, 2018.

*Valuation of Warrant Liability*

The warrant liability in the table above is composed of the fair value of warrants to purchase common shares that the Company issued to two of its directors in connection with a guarantee of its obligations under a credit agreement (see Note 9). On January 26, 2018, the anti-dilution price protection provisions contained within the warrants expired. Due to the expiration of these provisions, the Company discontinued classification of these warrants as a liability, and has accordingly reclassified them to additional paid-in capital within shareholders' equity. On expiration, the fair value of the warrant liability was determined based on significant inputs not observable in the market, which represents a Level 3 measurement within the fair value hierarchy.

The Company utilized the Black-Scholes option pricing model to value the warrant liability. The Black-Scholes option pricing model incorporated assumptions and estimates to value the warrant liability. Estimates and assumptions impacting the fair value measurement included the number of shares for which the warrants will be exercisable, the fair value per share of the underlying common shares issuable upon exercise of the warrants, the remaining contractual term of the warrants, the risk-free interest rate, the expected dividend yield, and the expected volatility of the price of the underlying common shares. The fair value per share of the Company's common shares was based on the closing trading price of the shares on January 26, 2018, the day of expiration, and the increase in the fair value of the common shares during the time period from December 31, 2017 to expiration is the primary reason for the increase in the fair value of the warrant liability during the same period. The Company was a private company prior to its IPO in May 2017 and therefore lacks company-specific historical and implied volatility information of its shares. Therefore, it estimated its expected share volatility based on the historical volatility of publicly traded peer companies for a term equal to the remaining contractual term of the warrants. The risk-free interest rate was determined by reference to the U.S. Treasury yield curve for time periods approximately equal to the remaining contractual term of the warrants. The Company estimated a 0% expected dividend yield based on the fact that the Company has never paid or declared dividends and does not intend to do so in the foreseeable future.

*Valuation of Derivative Liability*

The fair value of the derivative liability recognized in connection with the Company's license agreement with Yale (see Note 13) was determined based on significant inputs not observable in the market, which represents a Level 3 measurement within the fair value hierarchy. The fair value of the derivative liability was determined using a Monte-Carlo simulation, which is a statistical method used to generate a defined number of share price paths to develop a reasonable estimate of the range of the expected share prices. The Monte-Carlo simulation incorporated assumptions and estimates to value the derivative liability, including the amount of the payment, the settlement date, the trading price of the Company's common shares, the risk-free interest rate and the expected volatility of the price of the underlying common shares.

In April 2017, the agreement with Yale was amended such that if the change-of-control event was an IPO, the change-of-control payment would be due to Yale on the first trading day when Yale was free to sell its equity interest in the Company and the change-of-control fee would be reduced by the dollar value of Yale's equity interest in the Company on the first trading day when Yale was free to sell its equity interest in the Company. Yale's equity interest in the Company was subject to a lock-up agreement, which generally restricted Yale's shares from being traded until October 31, 2017 and accordingly, the amount due to Yale in connection with the change-of-control provision of the agreement, if any, would be determined upon expiration of the lock-up period. The Company continued to remeasure the derivative liability to fair value at each reporting date and recognized

**3. Fair Value of Financial Assets and Liabilities (Continued)**

any changes in the fair value of the derivative liability through October 31, 2017. The derivative liability as of December 31, 2018, and upon expiration of the lock-up period was determined to be $0 based on the value of the Company's shares on this date.

*Valuation of Contingent Equity Liability*

**BMS.** The fair value of the contingent equity liability recognized in connection with the Company's license agreement with BMS (see Note 13) was determined based on significant inputs not observable in the market, which represents a Level 3 measurement within the fair value hierarchy. The fair value of the contingent equity liability was determined using the probability-weighted expected returns method ("PWERM"), which considered as inputs the probability of occurrence of events that would trigger the issuance of shares, the expected timing of such events, the value of the contingently issuable equity and a risk-adjusted discount rate. As of December 31, 2016, the assumed probability of occurrence of the event that was most probable of triggering the issuance of shares was 75%, the expected timing of such an event was estimated to be less than one year, the value of the contingently issuable equity was $18,750 and the discount rate was assessed to be 0%. In connection with the closing of the IPO in May 2017, the conditions for issuing shares in connection with the contingent equity liability were satisfied, and accordingly, the Company issued 1,345,374 common shares to BMS. The contingent equity liability was adjusted to fair value immediately prior to the completion of the IPO, and upon issuance of the common shares, the contingent equity liability was reclassified to equity.

**AstraZeneca.** The fair value of the contingent equity liability recognized in connection with the Company's license agreement with AstraZeneca (see Note 13) was determined based on significant inputs not observable in the market, which represents a Level 3 measurement within the fair value hierarchy. The fair value of the contingent equity liability was determined using the PWERM, which considered as inputs the probability of occurrence of events that would trigger the issuance of shares, the expected timing of such events, the value of the contingently issuable equity and a risk-adjusted discount rate. The contingently issuable equity is issuable in two tranches, each for a fixed dollar amount of $5,000, for a total amount of $10,000. Using the PWERM, the Company assessed the fair value of each tranche of the contingent equity liability separately.

In October 2016, upon completion of the Series A First Closing (see Note 10), the first tranche of contingently issuable equity became issuable to AstraZeneca. As a result, the Company issued to AstraZeneca 538,150 Series A preferred shares with an aggregate fair value of $5,000, or $9.2911 per share, in satisfaction of the obligation to issue the first tranche of equity under the agreement. Upon the issuance of the 538,150 Series A preferred shares to AstraZeneca in October 2016, the Company reclassified the carrying value of the first tranche contingent equity liability, equal to the then-current fair value of $5,000, to the carrying value of Series A preferred shares.

The shares related to the second tranche became issuable upon the earlier of (i) the initiation of a Phase 2b or equivalent clinical trial of a product candidate based on the licensed patent rights and (ii) any liquidity event, including an IPO, any change of control or any assignment of the Company's rights or obligations under the license agreement. As of December 31, 2016, the Company determined that the fair value of the second tranche contingent equity liability was $4,875. In determining this fair value, the assumed probability of occurrence of the event that was most probable of triggering the issuance of shares was 65%, the expected timing of such an event was estimated to be less than one year, the value of the contingently issuable equity was $7,500 and the discount rate was assessed to be 0%. In connection with the closing of the IPO in May 2017, the conditions for issuing shares in connection with the contingent equity liability were satisfied, and accordingly, the Company issued 538,149 common shares to AstraZeneca. The contingent equity liability was adjusted to fair value immediately prior to the completion of the IPO, and upon issuance of the common shares, the contingent equity liability was reclassified to equity.

(Amounts in thousands, except share and per share amounts)

**3. Fair Value of Financial Assets and Liabilities (Continued)**

The following table provides a roll forward of the aggregate fair values of the Company's warrant liability, derivative liability and contingent equity liability, for which fair value is determined by Level 3 inputs:

| | Warrant Liability | Derivative Liability | Contingent Equity Liability |
|---|---|---|---|
| December 31, 2016 | 780 | 512 | 18,938 |
| Change in fair value | 3,241 | (512) | 13,082 |
| Issuance of common shares in settlement of contingent equity liability | — | — | (32,020) |
| December 31, 2017 | 4,021 | — | — |
| Change in fair value | 1,182 | — | — |
| Reclassification to equity | (5,203) | — | — |
| Balance as at December 31, 2018 | $ — | $ — | $ — |

*Beneficial Conversion Feature*

In connection with the second tranche closing of Series A preferred shares on February 17, 2017, the Company determined that the conversion option associated with the shares sold met the definition of a beneficial conversion feature ("BCF") as the fair value of the underlying common shares exceeded the adjusted conversion price. The BCF was recognized at its fair value of $12,006 as a reduction to the carrying value of the Series A preferred shares and a corresponding adjustment to additional paid-in capital. The fair value was determined using Level 3 inputs, equal to the product of the number of shares sold in the second tranche closing multiplied by the difference between the adjusted conversion price and the per share value of common shares at the commitment date (see Note 10). In May 2017, upon the completion of the Company's IPO, all of the outstanding Series A preferred shares were automatically converted into an aggregate of 9,358,560 common shares. Upon conversion of the Series A preferred shares, the remaining unamortized BCF was reclassified to additional paid-in capital as a deemed dividend.

**4. Prepaid Expenses and Other Current Assets**

Prepaid expenses and other current assets consisted of the following:

| | December 31, | |
|---|---|---|
| | 2018 | 2017 |
| Prepaid clinical trial costs | $ 7,210 | $ 4,642 |
| Prepaid insurance | 393 | 455 |
| Other | 487 | 100 |
| | $ 8,090 | $ 5,197 |

**5. Equity Method Investment**

On August 29, 2016, the Company executed a stock purchase agreement with Kleo Pharmaceuticals, Inc. ("Kleo"), a privately held Delaware corporation, to purchase 3,000,000 shares of Kleo's common stock at an initial closing, with a commitment to purchase an aggregate of 5,500,000 additional shares of common stock, in each case at a share price of $1.00 per share (the "Kleo SPA"). Kleo is a development-stage biopharmaceutical company focused on advancing the field of immunotherapy by developing small molecules that emulate biologics. The Company purchased 3,000,000 shares upon the initial closing on August 31, 2016, and the remaining 5,500,000 shares were to be purchased in four equal tranches of 1,375,000 shares beginning six months from the initial closing and then every three months thereafter. In connection with the initial investment, the Company received the right to designate two of the members of Kleo's board of directors. The Company completed all four of remaining tranche purchases in March, June, October 2017 and January 2018, with each tranche purchase consisting of 1,375,000 shares for cash consideration of $1,375.

In March 2017, the Company purchased 500,000 shares of Kleo common stock directly from a co-founder of Kleo for consideration of $250 in cash and 32,500 common shares of the Company.

(Amounts in thousands, except share and per share amounts)

**5. Equity Method Investment (Continued)**

In addition to these purchases, in October 2017, the Company purchased an additional aggregate of 2,049,543 shares for cash consideration of $2,253 which allowed the Company to maintain its relative ownership interest in Kleo. As of December 31, 2017, the Company's ownership interest in the outstanding stock of Kleo was 43.3%. Upon completion of the fourth and final tranche investment in January 2018, the Company's ownership increased to 46.6%.

In November 2018, the Company participated in Kleo's Series B funding raise. The Company purchased 1,420,818 shares for cash consideration of $5,000. As of the close of the Series B funding raise, and as of December 31, 2018, the Company's ownership interest in the outstanding common stock of Kleo was 41.9%.

The Company has a variable interest in Kleo through its equity investment. Kleo is a variable interest entity due to the equity investment at risk being insufficient to finance its activities. An assessment of whether or not the Company has the power to direct activities that most significantly impact Kleo's economic performance and to identify the party that obtains the majority of the benefits of the investment was performed as of December 31, 2018 and 2017, and will be performed as of each subsequent reporting date. After each of these assessments, the Company concluded that the activities that most significantly impact Kleo's economic performance are the ability to direct the research activities, the ability to select vendors to perform the research, the ability to maintain research staff and the ability to raise additional funds, each of which are directed by Kleo. Based on the outcome of these assessments, the Company concluded that the investment should be accounted for under the equity method.

The Company has recorded its investments in Kleo to date based on the costs of those investments, as adjusted for the Company's proportional share of Kleo's net income or loss in each period. The difference between the cost of the Company's investments in Kleo and its proportionate share of the net assets of Kleo was allocated to goodwill and indefinite-lived intangible assets. The Company records future adjustments to the carrying value of its investment at each reporting date equal to its proportionate share of Kleo's net loss for the corresponding period. The Company recorded other expense and a corresponding reduction in the carrying value of its investment in Kleo of $2,808 and $1,885 for its proportionate share of Kleo's net loss for the years ended December 31, 2018 and 2017, respectively.

The carrying value of the Company's investment in Kleo was $11,414 and $7,847 as of December 31, 2018 and 2017, respectively, and is reported as equity method investment on the consolidated balance sheet. The carrying value of the investment represents the Company's maximum loss exposure as of December 31, 2018.

The following table provides a roll forward of the carrying value of the Company's equity method investment:

| | Carrying Value |
|---|---|
| Balance as at December 31, 2016 | $ 2,753 |
| Purchase of Kleo common stock | 6,979 |
| Loss recognized in connection with equity method investment | (1,885) |
| Balance as at December 31, 2017 | 7,847 |
| Purchases of Kleo common stock | 6,375 |
| Loss recognized in connection with equity method investment | (2,808) |
| Balance as at December 31, 2018 | $ 11,414 |

Summarized financial information for Kleo is as follows:

| | December 31, | |
|---|---|---|
| | 2018 | 2017 |
| Current assets | $ 23,762 | $ 8,388 |
| Total assets | $ 24,048 | $ 8,746 |
| Current liabilities | $ 1,598 | $ 1,415 |
| Total liabilities | $ 2,054 | $ 4,201 |

(Amounts in thousands, except share and per share amounts)

**5. Equity Method Investment (Continued)**

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Revenue | $ — | $ — | $ — |
| Loss from operations | $ (6,501) | $ (5,646) | $ (3,764) |
| Net loss | $ (6,334) | $ (5,658) | $ (3,727) |

**6. Property and Equipment, Net**

Property and equipment, net consisted of the following:

| | December 31, | |
|---|---|---|
| | 2018 | 2017 |
| Building and Land | $ 2,200 | $ — |
| Building Improvements | 3,210 | — |
| Computer Hardware | 420 | 163 |
| Furniture & Fixtures | 280 | — |
| Office Equipment | 441 | 26 |
| | $ 6,551 | $ 189 |
| Accumulated depreciation | (303) | (43) |
| Construction in progress | — | 2,198 |
| | $ 6,248 | $ 2,344 |

In August 2017, the Company entered into a lease agreement to consolidate our headquarters into a free standing building in New Haven, Connecticut, which we began occupying during the fourth quarter of 2018. The Company had the option to purchase the property for $2,700 and executed that option in December 2018.

Depreciation expense was $261, $35 and $5 for the years ended December 31, 2018, 2017 and 2016, respectively. Assets under the Company's financing lease included in construction in progress were $0 and $1,787 as of December 31, 2018 and December 31, 2017, respectively (see Note 16).

**7. Accrued Expenses**

Accrued expenses consisted of the following:

| | December 31, | |
|---|---|---|
| | 2018 | 2017 |
| Accrued employee compensation and benefits | $ 108 | $ 89 |
| Accrued clinical trial costs | 6,753 | 3,582 |
| Accrued professional fees | 1,636 | 390 |
| Lease liability | — | 362 |
| Other | 285 | 285 |
| | $ 8,782 | $ 4,708 |

**(Amounts in thousands, except share and per share amounts)**

**8. Liability Related to Sale of Future Royalties**

In June 2018, pursuant to the Funding Agreement entered into by the Company and RPI, a Delaware statutory trust, the Company issued to RPI the right to receive certain revenue participation payments, subject to certain reductions, based on the future global net sales of the Products for each calendar quarter during the royalty term contemplated by the Funding Agreement ("Revenue Participation Right"), in exchange for $100,000 in cash. Specifically, the participation rate commences at 2.1% on annual global net sales of up to and equal to $1,500,000, declining to 1.5% on annual global net sales exceeding $1,500,000.

In addition, the Company had the option to repurchase 100% of the Revenue Participation Right from RPI for a purchase price of $155,000, if the Company entered into a definitive agreement to consummate a change of control. The Company did not exercise the Buy-Back Option which expired in July 2018.

Concurrent with the Funding Agreement, the Company entered into a Purchase Agreement with RPI. Pursuant to the Purchase Agreement, the Company sold 1,111,111 common shares of the Company to RPI at a price of $45.00 per share, for gross proceeds of $50,000.

The Company concluded that there were two units of accounting for the consideration received comprised of the liability related to sale of future royalties and the common shares. The Company allocated the $100,000 from the Funding Agreement and $50,000 from the Purchase Agreement among the two units of accounting on a relative fair value basis at the time of the transaction. The Company allocated $106,047 in transaction consideration to the liability, and $43,953 to the common shares. The Company determined the fair value of the common shares based on the closing stock price on the transaction date, adjusted for the trading restrictions. The transaction costs incurred related to the transactions with RPI of $377 were allocated in proportion to the allocation of total consideration to the two units of accounting. The effective interest rate under the Funding Agreement, including transaction costs, as of December 31, 2018 is approximately 22%.

The following table shows the activity within the liability related to sale of future royalties for the twelve months ended December 31, 2018:

| | | Liability Related to Sale of Future Royalties |
|---|---|---|
| Transaction date balance | $ | 106,047 |
| Non-cash interest expense recognized, net of transaction cost amortization | | 11,726 |
| Balance at December 31, 2018 | | 117,773 |
| Less: Unamortized transaction costs | | (258) |
| Carrying value at December 31, 2018 | $ | 117,515 |

**9. Warrants**

***Credit Agreement***

On August 30, 2016, the Company entered into a one-year credit agreement (the “Credit Agreement”) with Wells Fargo Bank, National Association (“Wells Fargo”) providing for a term loan in the principal amount of $5,000 (the “Loan”) and borrowed the full $5,000 available under the Credit Agreement. In connection with the agreement, the Company issued warrants to two members of the Company’s Board of Directors in exchange for providing a guarantee on the debt. The Credit Agreement was fully satisfied with a principal repayment to Wells Fargo of $5,000 on August 31, 2017.

The Company recognized interest expense of $906 and $385 during the twelve months ended months ended December 31, 2017 and 2016, respectively. The Company recognized $784 and $347 related to the accretion of the debt discount during the twelve months ended December 31, 2017 and 2016, respectively.

***Notes Payable to Related Parties***

On December 31, 2016, the Company entered into stock purchase agreements with each of the stockholders of Biohaven Pharmaceuticals, Inc. ("BPI"), acquiring 100% of the issued and outstanding shares of BPI for aggregate purchase consideration of $595. The Company funded the acquisition through the issuance of promissory notes to each of the former stockholders of BPI. The former stockholders of BPI are shareholders of the Company and also serve as the Company's Chairman of the board

(Amounts in thousands, except share and per share amounts)

**9. Warrants (Continued)**

of directors, Chief Executive Officer, and Chief Medical Officer, respectively. The notes were payable in five annual payments, the first four of which were interest only, with the final payment to include the principal balance outstanding plus any accrued and unpaid interest. The notes bore interest at a rate of 4.5% per annum and had a maturity date of December 31, 2021. The notes became immediately due and payable upon specified events, including immediately prior to the consummation of an initial public offering of the Company's common shares or upon the occurrence of a change of control of the Company.

In connection with the closing of the Company's IPO in May 2017, the notes were paid in full.

***Guarantor and Co-Guarantor Warrants***

In connection with entering into the Credit Agreement, the Company issued warrants to purchase common shares to two of the Company's directors in connection with a guarantee of its obligations under the agreement. The Company previously classified the warrants as a liability on its consolidated balance sheet because each warrant represented a freestanding financial instrument that was not indexed to the Company's own shares. The warrant liability was initially recorded at fair value upon entering into the credit agreement and was subsequently remeasured to fair value at each reporting date. Changes in the fair value of the warrant liability was recognized as a component of other income (expense), net in the consolidated statement of operations and comprehensive loss.

On January 26, 2018, the anti-dilution price protection provisions contained within the warrants issued to each of the guarantor and co-guarantor of the Credit Agreement expired. Both the guarantor and co-guarantor are members of the Company's Board of Directors.

Changes in the fair value of the warrant liability, until expiration of the anti-dilution price protection provisions, are recognized as a component of other income (expense), net, in the Company's consolidated statement of operations and comprehensive loss. Upon expiration of the provision, the Company discontinued classification of these warrants as a liability, and has accordingly reclassified the fair value of $5,203 to additional paid-in capital within shareholders' equity.

The fair value of the warrant liability was $4,021 at December 31, 2017. The following table provides income (expense) related to the warrant liability which the Company records net within other income (expense) in the consolidated statements of operations:

| | Twelve Months Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Income (expense) from change in fair value of warrant liability | $ (1,182) | $ (3,241) | $ 154 |

**10. Convertible Preferred Shares**

In October 2016, the Company issued and sold an aggregate of 4,305,209 Series A preferred shares (the "Series A First Closing"). The preferred share purchase agreement provided for the issuance of additional Series A preferred shares in a second and final tranche (the "Series A Second Closing"). Also, in October 2016, the Company issued 538,150 Series A preferred shares in satisfaction of the obligation to issue the first tranche of contingently issuable equity under the Company's license agreement with AstraZeneca.

In February 2017, the Company completed the Series A Second Closing through the issuance and sale of an aggregate of 4,305,182 Series A preferred shares. The conversion option associated with the Series A preferred shares sold in the second closing met the definition of a BCF as the fair value of the underlying common shares exceeded the stated conversion price. Upon the sale and issuance of the Series A preferred shares, $2,406 of the BCF was immediately accreted, as this represented the difference between the stated conversion price and per share value of the common shares. The remaining portion of the BCF was being amortized using the effective interest method over the period from the date of issuance to the date of the earliest possible conversion, October 1, 2017.

In May 2017, upon the completion of the Company's IPO, all of the outstanding Series A preferred shares were automatically converted into an aggregate of 9,358,560 common shares. Upon conversion of the Series A preferred shares, the remaining unamortized BCF was reclassified to additional paid-in capital as a deemed dividend.

**11. Common Shares**

As of December 31, 2016, the Company had authorized the Company to issue 38,000,000 no par value common shares. On April 21, 2017, the Company effected an increase in the number of authorized common shares to 50,000,000 shares. Additionally, in connection with the completion of its IPO in May 2017, the Company amended its memorandum and articles of association to authorize the issuance of up to 200,000,000 no par value common shares.

Each common share entitles the holder to one vote on all matters submitted to a vote of the Company's shareholders. Common shareholders are entitled to receive dividends, as may be declared by the board of directors.

In February 2016, the Company issued 429,000 common shares at an issuance price of $7.00 per share for proceeds of $2,980, net of issuance costs of $23.

In May 2016 and July 2016, the Company issued an aggregate of 1,090,500 common shares at an issuance price of $7.70 per share for proceeds of $8,299, net of issuance costs of $97.

In July 2016, concurrently with the issuance of the Company's common shares to Connecticut Innovations Incorporated ("CII"), the Company and CII entered into a put agreement (the "Put Agreement"). The Put Agreement grants CII the right to sell (the "Put Option") to the Company all or any part of CII's warrant rights (if any), shares (if any) or notes (if any). The Put Option becomes exercisable upon the Company's breach of the covenant to maintain a presence in Connecticut, as defined in the Put Agreement. The right to put the shares terminated on October 31, 2017, upon expiration of the lock-up period following the completion of the Company's IPO.

On May 3, 2017, the Company's registration statement on Form S-1 relating to the IPO was declared effective by the SEC. The IPO closed on May 9, 2017 and the Company issued and sold 9,900,000 common shares at a public offering price of $17.00 per share for net proceeds of $152,651 after deducting underwriting discounts and commissions of $11,781 and other offering expenses of $3,868. Upon the closing of the IPO, all convertible preferred shares then outstanding converted into an aggregate of 9,358,560 common shares. In addition, on May 9, 2017, the underwriters of the IPO fully exercised their option to purchase additional shares, and on May 11, 2017, the Company issued and sold 1,485,000 common shares for net proceeds of $23,478 after deducting underwriting discounts and commissions of $1,767. The aggregate net proceeds to the Company from the IPO, after deducting underwriting discounts and commissions and offering expenses, were $176,128.

In connection with the completion of its IPO, the Company issued an aggregate of 1,883,523 common shares to BMS and AstraZeneca in satisfaction of obligations to contingently issue equity securities pursuant to the license agreements (see Note 13), for no additional consideration.

In December 2018, we closed on an underwritten public offering of 3,859,060 of common shares, including the full exercise of the underwriters' option to purchase additional shares, at a price to the public of $37.25 per share. The aggregate gross proceeds to the Company from the offering, before deducting the underwriting discounts and commissions and offering expenses payable, were approximately $143,750.

***Private Placements***

In March 2018, the Company sold an aggregate of 2,000,000 common shares in a private placement at a price of $27.50 per share, for net proceeds of $52,000 (“Private Placement”) after deducting underwriting discounts and commissions of $2,800 and other offering expenses of $200. Subsequent to the closing of the Private Placement, the Company paid BMS the $50,000 upfront payment under the BMS Amendment (see Note 13).

In June 2018, pursuant to the Purchase Agreement between the Company and RPI (Note 8), the Company sold 1,111,111 common shares to RPI at a price of $45.00 per common share for net proceeds of $49,889 after deducting offering expenses of $111.

***2018 License Agreement with AstraZeneca***

In September 2018, the Company entered into a License Agreement (the “2018 AstraZeneca Agreement”) with AstraZeneca AB (“AstraZeneca”). Under the 2018 AstraZeneca Agreement, the Company paid AstraZeneca an upfront cash payment of $3,000 and 109,523 shares valued at $4,080 on the settlement date (see Note 13).

**11. Common Shares (Continued)**

***Agreement with ALS Biopharma, LLC and Fox Chase Chemical Diversity Center Inc.***

In January 2018, ALS Biopharma exercised a warrant for the purchase of 275,000 shares through a net share settlement, resulting in an issuance of 228,219 shares.

In April 2018, ALS Biopharma exercised a warrant for the purchase of 325,000 shares through a net share settlement, resulting in an issuance of 261,140 shares.

**12. Share-Based Compensation**

***2014 Equity Incentive Plan***

The Company's 2014 Equity Incentive Plan, as amended (the "2014 Plan"), provided for the Company to sell or issue common shares or restricted common shares, or to grant incentive stock options or nonqualified stock options for the purchase of common shares, to employees, members of the board of directors and consultants of the Company. The exercise prices, vesting and other restrictions are determined at the discretion of the board of directors, or their committee if so delegated, except that the exercise price per share of stock options may not be less than 100% of the fair market value of the common share on the date of grant and the term of stock option may not be greater than 10 years.

The total number of common shares that may be issued under the 2014 Plan was 4,000,000 shares as of December 31, 2016. In January 2017, the Company effected an increase, effective October 28, 2016, in the number of common shares reserved for issuance under the 2014 Plan from 4,000,000 to 4,899,230 shares.

Upon effectiveness of the 2017 Plan, there are no further shares authorized for grant under the 2014 Plan.

***2017 Equity Incentive Plan***

In April 2017, the Company's shareholders approved the 2017 Equity Incentive Plan (the "2017 Plan"), which became effective on May 3, 2017 in connection with the Company's IPO. The 2017 Plan provides for the grant of incentive share options, nonstatutory share options, share appreciation rights, restricted share awards, restricted share unit awards, performance-based share awards and other share-based awards. Additionally, the 2017 Plan provides for the grant of performance cash awards. Upon the effectiveness of the 2017 Plan, there were 2,713,113 shares authorized for issuance under the 2017 Plan. As of December 31, 2017, 1,138,903 shares remained available for future grant under the 2017 Plan. In January 2018, the Board of Directors approved an additional 1,437,227 shares to be issued under the 2017 Plan. As of December 31, 2018, 681,307 shares remained available for future grant under the 2017 Plan. In January 2019, the Board of Directors approved an additional 1,767,901 shares to be issued under the 2017 Plan.

Vesting periods are determined at the discretion of the board of directors. Stock options typically vest over three or four years. The maximum contractual term is 10 years.

During the years ended December 31, 2018, 2017 and 2016 the Company granted options to purchase 1,810,000, 2,335,106 and 417,875 common shares to employees and directors, respectively. The Company recorded non-cash share-based compensation expense for options granted to employees and directors of $11,246, $5,210 and $2,284 during the years ended December 31, 2018, 2017 and 2016, respectively.

During the year ended December 31, 2018, 2017 and 2016 the Company granted options to purchase 145,000, 273,537 and 199,050 common shares to non-employees, respectively. The Company recorded non-cash share-based compensation expense for options granted to non-employees of $5,679, $8,029 and $2,319 during the years ended December 31, 2018, 2017 and 2016, respectively. The Company measures and records the value of non-employee options over the period of time services are provided and, as such, unvested portions are subject to remeasurement at subsequent reporting periods.

(Amounts in thousands, except share and per share amounts)

**12. Share Based Compensation (Continued)**

***Stock Option Valuation***

The assumptions that the Company used to determine the grant-date fair value of stock options granted to employees and directors under the 2014 Plan and the 2017 Plan (collectively, the "Plans") were as follows, presented on a weighted average basis:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Risk-free interest rate | 2.91 % | 2.10 % | 2.19 % |
| Expected term (in years) | 6.25 | 6.02 | 5.75 |
| Expected volatility | 73.03 % | 73.26 % | 70.58 % |
| Expected dividend yield | — % | — % | — % |
| Exercise price | $ 32.35 | $ 18.47 | $ 9.29 |

The assumptions that the Company used to determine the grant-date fair value of stock options granted to non-employees under the Plans were as follows, presented on a weighted average basis:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Risk-free interest rate | 3.06 % | 2.35 % | 2.54 % |
| Expected term (in years) | 10 | 10 | 10 |
| Expected volatility | 74.50 % | 71.12 % | 67.16 % |
| Expected dividend yield | — % | — % | — % |
| Exercise price | $ 32.42 | $ 18.23 | $ 9.29 |

***Stock Options***

Stock option activity under the Plans is summarized as follows:

| | Number of Shares | Weighted Average Exercise Price | Weighted Average Remaining Contractual Term (in years) | Aggregate Intrinsic Value |
|---|---|---|---|---|
| Outstanding as of December 31, 2017 | 6,151,643 | $ 9.97 | 8.42 | $ 107,072 |
| Granted | 1,955,000 | $ 32.35 | 9.70 | |
| Exercised | (577,288) | $ 6.26 | | |
| Forfeited | (85,176) | $ 22.54 | | |
| Outstanding as of December 31, 2018 | 7,444,179 | $ 15.99 | 8.05 | $ 156,518 |
| Options exercisable as of December 31, 2018 | 3,854,598 | $ 6.26 | 6.92 | $ 118,452 |
| Options unvested as of December 31, 2018 | 3,589,581 | $ 26.46 | 9.26 | $ 38,066 |

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common shares for those stock options that had exercise prices lower than the fair value of the Company's common shares. The total intrinsic value of stock options for the years ended December 31, 2018, 2017 and 2016 was $156,518, $107,072 and $15,991, respectively.

The weighted average grant-date fair value per share of stock options granted for the years ended December 31, 2018, 2017 and 2016 was $22.00, $12.31 and $4.09, respectively.

The total fair value of options vested for the years ended December 31, 2018, 2017 and 2016 was $25,876, $15,494 and $3,381, respectively.

(Amounts in thousands, except share and per share amounts)

**12. Share Based Compensation (Continued)**

***Non-Cash Share-Based Compensation***

Non-cash share-based compensation expense was classified in the consolidated statements of operations and comprehensive loss as follows:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Research and development expenses | $ 8,371 | $ 6,933 | $ 2,382 |
| General and administrative expenses | 8,554 | 6,306 | 2,221 |
| | $ 16,925 | $ 13,239 | $ 4,603 |

As of December 31, 2018, total unrecognized compensation cost related to the unvested share-based awards was $61,583, which is expected to be recognized over a weighted average period 3.30 years.

**13. License and Other Agreements**

***Yale Agreement***

In September 2013, the Company entered into an exclusive license agreement with Yale (the "Yale Agreement") to obtain a license to certain patent rights for the commercial development, manufacture, distribution, use and sale of products and processes resulting from the development of those patent rights, related to the use of riluzole in treating various neurological conditions, such as general anxiety disorder, post-traumatic stress disorder and depression. As part of the consideration for this license, the Company issued Yale 250,000 common shares and granted Yale the right to purchase up to 10% of the securities issued in specified future equity offerings by the Company, in addition to the obligation to issue shares to prevent anti-dilution. The obligation to contingently issue equity to Yale, which was no longer outstanding as of December 31, 2018, was determined to be a liability, which was accounted for at its fair value of zero at each reporting date.

The Yale Agreement provided for a change-of-control payment to Yale upon the occurrence of a change-of-control event, as defined in the agreement, including an IPO. Upon the occurrence of a change-of-control event, the Company was obligated to pay to Yale the lesser of (i) 5% of the dollar value of all initial and future potential consideration paid or payable by the acquirer or (ii) $1,500. If the change-of-control event was an IPO, the amount the Company would have been obligated to pay to Yale would have been reduced by the value of Yale's equity investment in the Company on the first day that Yale was free to sell its equity interest. The Company classified the change-of-control payment obligation as a liability on its consolidated balance sheet because it represented a contingent obligation to pay a variable amount of cash that may be based, in part, on the value of the Company's own shares. The issuance date fair value of the derivative liability of $14 was recognized as a research and development expense upon entering the agreement with Yale. The Company continued to remeasure the derivative liability to fair value at each reporting date and recognized changes in the fair value of the derivative liability through October 31, 2017. The derivative liability upon expiration of the lock-up period was determined to be $0 based on the value of the Company's shares on that date.

The Company recorded other income (expense) of $0, $512 and $(65) during the years ended December 31, 2018, 2017 and 2016, respectively, for the change in the fair value of the derivative liability. The fair value of the derivative liability was $0 and $0 as of December 31, 2018 and 2017, respectively (see Note 3).

In addition, the Company agreed to pay Yale up to $2,000 upon the achievement of specified regulatory milestones and annual royalty payments of a low single-digit percentage based on net sales of products from the licensed patents, subject to a minimum amount of up to $1,000 per year. If the Company grants any sublicense rights under the Yale Agreement, it must pay Yale a low single-digit percentage of sublicense income that it receives. To date, no milestone or royalty payments have been made under this agreement.

The Yale Agreement also requires the Company to meet certain due diligence requirements based upon specified milestones. The Company can elect to extend the deadline for its compliance with the due diligence requirements by a maximum of one year upon the payment to Yale of up to $150. The Company is also required to reimburse Yale for any fees that Yale incurs related to the filing, prosecution, defending and maintenance of patent rights licensed under the Yale Agreement. In the event that the Company fails to make any payments, commits a material breach, fails to maintain adequate insurance or challenges the patent rights of Yale, Yale can terminate the Yale Agreement. The Company can terminate the Yale

**13. License and Other Agreements (Continued)**

Agreement (i) upon 90 days' notice to Yale, (ii) if Yale commits a material breach of the Yale Agreement or (iii) as to a specific country if there are no valid patent rights in such country. The Yale Agreement expires on a country-by-country basis upon the later of the date on which the last patent rights expire in such country or ten years from the date of the first sale of a product incorporating the licensed patents.

***MGH Agreement***

In September 2014, the Company entered into a license agreement (the "MGH Agreement") with The General Hospital Corporation d/b/a Massachusetts General Hospital ("MGH"), pursuant to which MGH granted the Company a license to certain patent rights for the commercial development, manufacture, distribution and use of any products or processes resulting from development of those patent rights, related to treating depression with a combination of ketamine and scopolamine. The Company is also obligated to pay MGH annual license maintenance fees and future milestone payments of up to $750 upon the achievement of specified clinical and regulatory milestones and up to $2,500 upon the achievement of specified commercial milestones. The Company has also agreed to pay MGH royalties of a low single-digit percentage based on net sales of products licensed under the agreement. If the Company receives revenue from sublicensing any of its rights under the agreement, the Company is also obligated to pay a portion of that revenue to MGH. To date, no milestone payments have been made under this agreement.

The MGH Agreement also requires the Company to meet certain due diligence requirements based upon specified milestones. The Company can elect to extend the deadline for its compliance with the due diligence requirements by a maximum of one year by making payments to MGH of up to $300 in the aggregate. The Company is required to reimburse MGH for any fees that MGH incurs related to the filing, prosecution, defending, and maintenance of patent rights licensed under the agreement. The MGH Agreement expires upon expiration of the patent rights under the MGH Agreement, unless earlier terminated by either party.

***ALS Biopharma Agreement***

In August 2015, the Company entered into an agreement (the "ALS Biopharma Agreement") with ALS Biopharma and Fox Chase Chemical Diversity Center Inc. ("FCCDC"), pursuant to which ALS Biopharma and FCCDC assigned the Company their worldwide patent rights to a family of over 300 prodrugs of glutamate modulating agents, including troriluzole, as well as other innovative technologies. Under the ALS Biopharma Agreement, the Company is obligated to use commercially reasonable efforts to commercialize and develop markets for the patent products. The Company is obligated to pay $3,000 upon the achievement of specified regulatory milestones with respect to the first licensed product and $1,000 upon the achievement of specified regulatory milestones with respect to subsequently developed products, as well as royalty payments of a low single-digit percentage based on net sales of products licensed under the agreement, payable on a quarterly basis. To date, no milestone or royalty payments have been made under this agreement.

In connection with the ALS Biopharma Agreement, the Company also issued to ALS Biopharma (i) 50,000 common shares; (ii) an immediately exercisable warrant to purchase 275,000 common shares at an exercise price of $5.60 per share; and (iii) a warrant to purchase 325,000 common shares at an exercise price of $5.60 per share, which warrant would become exercisable upon the Company's achievement of a specified regulatory milestone which was met in May 2016 (see Note 9). The ALS Biopharma Agreement terminates on a country-by-country basis as the last patent rights expire in each such country. If the Company abandons its development, research, licensing or sale of all products covered by one or more claims of any patent or patent application assigned under the ALS Biopharma Agreement, or if the Company ceases operations, it has agreed to reassign the applicable patent rights back to ALS Biopharma.

The Company recorded research and development expenses of $0, $0 and $3,127 during the years ended December 31, 2018, 2017 and 2016, respectively, as a result of the ALS Biopharma Agreement, which amounts consist of the fair value of the shares and warrants upon their issuance to ALS Biopharma.

***Rutgers Agreement***

In June 2016, the Company entered into an exclusive license agreement (the "Rutgers Agreement") with Rutgers, The State University of New Jersey ("Rutgers"), licensing several patents and patent applications related to the use of riluzole to treat various cancers. Under the Rutgers Agreement, the Company is required to pay Rutgers annual license maintenance fees until the first commercial sale of a licensed product, at which point the Company will pay Rutgers minimum annual royalties. The Company is also obligated to pay Rutgers up to $825 in the aggregate upon the achievement of specified clinical and

**13. License and Other Agreements (Continued)**

regulatory milestones. The Company agreed to pay Rutgers royalties of a low single-digit percentage of net sales of licensed products sold by the Company, its affiliates or its sublicensees, subject to a minimum amount of up to $100 per year. If the Company grants any sublicense rights under the Rutgers Agreement, the Company must pay Rutgers a low double-digit percentage of sublicense income it receives.

Under the Rutgers Agreement, in the event that the Company experiences a change of control or sale of substantially all of its assets prior to the initiation of a Phase 3 clinical trial related to products licensed under the agreement, and such change of control or sale results in a full liquidation of the Company, the Company will be obligated to pay Rutgers a change-of-control fee equal to 0.30% of the total value of the transaction, but not less than $100. The Company determined that the change-of-control payment should be accounted for as a liability. The fair value of the obligation for all periods presented was $0 based on the Company's assessment that the probability of a change-in-control event occurring prior to the initiation of a Phase 3 clinical trial related to products licensed under the agreement was remote.

The Rutgers Agreement also requires the Company to meet certain due diligence requirements based upon specified milestones. The Company can elect to extend the deadline for its compliance with the due diligence requirements by a maximum of one year upon payments to Rutgers of up to $500 in the aggregate. Under the Rutgers Agreement, the Company is required to reimburse Rutgers for any fees that Rutgers incurs related to the filing, prosecution, defending, and maintenance of patent rights licensed under the agreement. The Rutgers Agreement expires upon expiration of the patent rights under the agreement or ten years from the date of first commercial sale of a licensed product, whichever is later, unless terminated by either party.

***BMS Agreement***

In July 2016, the Company entered into an exclusive, worldwide license agreement with BMS (the "BMS Agreement") for the development and commercialization rights to rimegepant and BHV-3500, as well as other CGRP-related intellectual property. In exchange for these rights, the Company agreed to pay BMS initial payments, milestone payments and royalties on net sales of licensed products under the agreement.

The Company is obligated to make milestone payments to BMS upon the achievement of specified development and commercialization milestones. The development milestone payments due under the agreement depend on the licensed product being developed. With respect to rimegepant, the Company is obligated to pay up to $127,500 in the aggregate upon the achievement of the development milestones. For any product other than rimegepant, the Company is obligated to pay up to $74,500 in the aggregate upon the achievement of the development milestones. In addition, the Company is obligated to pay up to $150,000 for each licensed product upon the achievement of commercial milestones. If the Company receives revenue from sublicensing any of its rights under the agreement, it is also obligated to pay a portion of that revenue to BMS. The Company is also obligated to make tiered royalty payments to BMS based on annual worldwide net sales, with percentages in the low to mid-teens.

Under the BMS Agreement, the Company is obligated to use commercially reasonable efforts to develop licensed products and to commercialize at least one licensed product using the patent rights licensed from BMS and is solely responsible for all development, regulatory and commercial activities and costs. The Company is also required to reimburse BMS for any fees that BMS incurs related to the filing, prosecution, defending, and maintenance of patent rights licensed under the BMS Agreement. Under the BMS Agreement, BMS transferred to the Company manufactured licensed products, including certain materials that will be used by the Company to conduct clinical trials.

The BMS Agreement will terminate on a licensed product-by-licensed product and country-by-country basis upon the expiration of the royalty term with respect to each licensed product in each country. BMS has the right to terminate the agreement upon the Company's insolvency or bankruptcy, the Company's uncured material breach of the agreement, including the failure to meet its development and commercialization obligations, or if the Company challenges any of BMS's patent rights. The Company has the right to terminate the BMS Agreement if BMS materially breaches the agreement or if, after the Company provides notice, it chooses not to move forward with development and commercialization in a specific country.

The BMS Agreement required the Company to complete a financing transaction with gross proceeds of at least $30,000, of which a minimum of $22,000 was to be from investment in equity prior to October 17, 2016, unless extended by mutual agreement of the Company and BMS. The BMS Agreement was amended, effective October 14, 2016, to extend the deadline

**13. License and Other Agreements (Continued)**

for completing the financing transaction to October 31, 2016, on which date the Series A First Closing was completed (see Note 13).

Under the BMS Agreement, the Company also agreed to issue BMS common shares in the amount of $12,500, which shares are contingently issuable upon the earliest to occur of (i) the initiation of a Phase 3 trial for the first licensed compound to reach such milestone, (ii) the Company's IPO or (iii) an event resulting in the change of control of the Company. Under the terms of the BMS Agreement, if the qualifying financing transaction involves the issuance of preferred shares, BMS is entitled to receive preferred shares instead of common shares, at its option. BMS also had the right to purchase up to 8%, on a fully diluted basis, of shares issued in a qualifying financing transaction (as defined in the BMS Agreement) on the same terms and rights as all other investors involved in the financing. The number of shares issuable to BMS under the agreement will be determined by dividing $12,500 by a price per share equal to the lower of (i) the price per share paid by investors in the Series A First Closing, or $9.2911 (see Note 13), or (ii) the price per share paid by investors in any subsequent financing event that occurs prior to the events specified above.

The obligation to contingently issue equity to BMS is classified as a liability on the consolidated balance sheet because it represents an obligation to issue a variable number of shares for a fixed dollar amount. Upon entering into the BMS Agreement, the issuance-date fair value of the contingent equity liability of $13,125 was recognized as research and development expense in the consolidated statement of operations and comprehensive loss. The Company remeasured the fair value of the contingent equity liability at each reporting date since the date of issuance, recognizing changes in the fair value of the contingent equity liability as a component of other income (expense), net in the consolidated statement of operations and comprehensive loss. Changes in the fair value of the contingent equity liability continued to be recognized until the occurrence of a triggering event, which occurred in May 2017 with the completion of the IPO.

In May 2017, in connection with the completion of its IPO, the Company issued 1,345,374 common shares to BMS in satisfaction of its obligation to contingently issue equity securities pursuant to the license agreement and remeasured the contingent equity liability to fair value. The Company recognized expense of $0, $8,809 and $13,125 during the years ended December 31, 2018, 2017 and 2016, respectively, as a result of changes to the fair value of the contingent equity liability prior to its extinguishment in May 2017.

The Company recorded $2,000 and $5,000 of research and development expense related to the BMS Agreement during the year ended December 31, 2018 and 2017, respectively, for the achievement of specified milestones.

***Amendment to License Agreement with BMS***

In March 2018, the Company entered into an Amendment to License Agreement with BMS (the “BMS Amendment”), which amends the License Agreement between the Company and BMS from July 2016 (the “Original License Agreement” and, as amended by the BMS Amendment, the “BMS License Agreement”). Under the BMS Amendment, the Company paid BMS an upfront payment of $50,000 in return for a low single-digit reduction in the royalties payable on net sales of rimegepant and a mid single-digit reduction in the royalties payable on net sales of BHV-3500, recorded in Research and Development expense in the Consolidated Statements of Operations and Comprehensive Loss. Under the Original License Agreement, the Company was obligated to make tiered royalty payments based on annual worldwide net sales of licensed products upon their approval and commercialization, with percentages in the low- to mid-teens.

The BMS Amendment also removes BMS’s right of first negotiation to regain its intellectual property rights or enter into a license agreement with the Company following the Company’s receipt of topline data from its Phase 3 clinical trials with rimegepant, and clarifies that antibodies targeting CGRP are not prohibited as competitive compounds under the non-competition clause of the Original License Agreement.

The BMS License Agreement continues to provide the Company with exclusive global development and commercialization rights to rimegepant, BHV-3500 and related CGRP molecules, as well as related know-how and intellectual property. The Company’s obligations to make development and commercial milestone payments to BMS under the Original License Agreement remain unchanged.

***2016 AstraZeneca Agreement***

In October 2016, the Company entered into an exclusive license agreement (the "2016 AstraZeneca Agreement") with AstraZeneca, pursuant to which AstraZeneca granted the Company a license to certain patent rights for the commercial development, manufacture, distribution and use of any products or processes resulting from development of those patent rights,

**13. License and Other Agreements (Continued)**

including BHV-5000 and BHV-5500. In exchange for these rights, the Company agreed to pay AstraZeneca an upfront payment, milestone payments and royalties on net sales of licensed products under the agreement. The regulatory milestones due under the agreement depend on the indication of the licensed product being developed as well as the territory where regulatory approval is obtained. Development milestones due under the agreement with respect to Rett syndrome total up to $30,000, and, for any indication other than Rett syndrome, total up to $60,000. Commercial milestones are based on net sales of all products licensed under the agreement and total up to $120,000. The Company has also agreed to pay tiered royalties based on net sales of all products licensed under the agreement of mid-single-digit to low double-digit percentages. If the Company receives revenue from sublicensing any of its rights under the 2016 AstraZeneca Agreement, the Company is also obligated to pay a portion of that revenue to AstraZeneca. To date, no payments have been made related to these milestones or royalties. The Company is also required to reimburse AstraZeneca for any fees that AstraZeneca incurs related to the filing, prosecution, defending, and maintenance of patent rights licensed under the 2016 AstraZeneca Agreement.

The 2016 AstraZeneca Agreement expires upon the expiration of the patent rights under the agreement, unless earlier terminated by either party, or on a country-by-country basis ten years after the first commercial sale.

As part of the consideration under the 2016 AstraZeneca Agreement, the Company agreed to issue to AstraZeneca common shares in the amount of $10,000 if the Company completed a qualifying equity financing resulting in proceeds of at least $30,000 prior to December 29, 2016. Under the terms of the 2016 AstraZeneca Agreement, if the qualifying financing transaction involved the issuance of preferred shares, AstraZeneca would be entitled to receive preferred shares instead of common shares, at its option. The number of shares issued would be determined based on the price per share paid by investors in the qualifying financing transaction. Upon the occurrence of the qualifying financing transaction, 50% of the shares would be issuable upon the closing of the transaction (the "First Tranche") and the other 50% would become issuable upon the earlier of (i) the initiation of a Phase 2b or equivalent clinical trial of a product candidate based on the licensed patent rights or (ii) any liquidity event, including an IPO of the Company, any change of control of the Company or any assignment of the Company's rights and obligations under the 2016 AstraZeneca Agreement (the "Second Tranche"). The number of shares issuable to AstraZeneca in each of the First Tranche and the Second Tranche is determined by dividing $5,000 by the price per share paid by investors in the Company's Series A First Closing, or $9.2911 (see Note 11). In addition, AstraZeneca had the right to purchase up to 8%, on a fully diluted basis, of shares issued in such qualifying financing transaction, on the same terms and rights as all other investors involved in the financing.

In October 2016, upon completion of the Series A First Closing (see Note 11), the contingency associated with the First Tranche of contingently issuable equity related to the occurrence of a qualified financing was satisfied. As a result, the Company issued to AstraZeneca 538,150 Series A preferred shares with an aggregate fair value of $5,000, or $9.2911 per share. Upon issuance of the 538,150 Series A preferred shares to AstraZeneca, the Company reclassified the contingent equity liability associated with the First Tranche of $5,000 to the carrying value of Series A preferred shares.

The Company determined that the fair value of the contingent equity liability associated with the Second Tranche at each reporting date since the date of issuance, recognizing changes in the fair value of the contingent equity liability as a component of other income (expense), net in the consolidated statement of operations and comprehensive loss. Changes in the fair value of the contingent equity liability continued to be recognized until the occurrence of a triggering event, which occurred in May 2017 with the completion of the IPO.

In May 2017, in connection with the completion of its IPO, the Company issued 538,149 common shares to AstraZeneca in satisfaction of its obligation to contingently issue the Second Tranche of equity securities pursuant to the license agreement and remeasured the contingent equity liability to fair value. The Company recognized expense of $4,273 and $938 during the years ended December 31, 2017 and 2016, respectively, as a result of changes to the fair value of the contingent equity liability prior to its extinguishment in May 2017.

***RPharm Agreement***

In November 2017, the Company entered into a consulting agreement with R PHARM US related to the commercial preparation for BHV-0223. In addition to fixed quarterly consulting expenses under the agreement, the Company agreed to pay up to $2,500 upon achievement of specific commercial milestones. During the year ended December 31, 2018 the Company paid $1,400 to R PHARM US under this agreement.

**13. License and Other Agreements (Continued)**

***Catalent Agreements for Rimegepant***

In January 2018, the Company entered into an exclusive world-wide license and development agreement with Catalent, Inc. pursuant to which the Company obtained certain license rights to the Zydis ODT technology for use with rimegepant. If the Company obtains regulatory approval or launches a rimegepant product that utilizes the Zydis ODT technology, the Company is obligated to pay Catalent up to $1,500 upon the achievement of specified regulatory and commercial milestones. If the Company commercializes a rimegepant product that utilizes the Zydis ODT technology, the agreement permits the Company to purchase the commercial product from Catalent at a fixed price, inclusive of a royalty. Under the agreement, Catalent will not develop or manufacture a formulation of any oral CGRP compound using Zydis ODT technology for itself or a third party until 2031, subject to certain minimum commercial revenues.

Under this agreement, the Company is responsible for conducting clinical trials and preparing and filing regulatory submissions. The Company has the right to sublicense its rights under the agreement subject to Catalent's prior written consent. Catalent has the right to enforce the patents covering the Zydis technology and to defend any allegation that a formulation using Zydis technology, such as rimegepant, infringes a third party's patent.

This agreement terminates on a country-by-country basis upon the later of (i) 10 years after the launch of the most recently launched product in such country and (ii) the expiration of the last valid claim covering each product in such country, unless earlier voluntarily terminated by the Company. This agreement automatically extends for one-year terms unless either party gives advance notice of intent to terminate. In addition, Catalent may terminate the agreement either in its entirety or terminate the exclusive nature of this agreement on a country-by-country basis if the Company fails to meet specified development timelines, which it may extend in certain circumstances.

In July 2018, the Company entered into a commercial supply agreement with Catalent pursuant to which Catalent will exclusively manufacture and supply the Company's worldwide requirements for rimegepant in the Zydis ODT delivery formulation, if the Company pursues and receives regulatory approval of this formulation of rimegepant, for an initial term of five years after its commercial launch with optional two-year renewal periods. Under the agreement, Catalent will supply the rimegepant Zydis ODT product at a fixed price, inclusive of a royalty, and will not develop or manufacture a formulation of any oral CGRP compound using Zydis ODT technology for itself or a third party for a specified period of time, subject to certain minimum commercial revenues.

***Revenue Participation Right with RPI Finance Trust***

In June 2018, pursuant to the Funding Agreement entered into by the Company and RPI (Note 8), the Company granted to RPI the right to receive certain revenue participation payments, subject to certain reductions, based on the future global net sales of the Products, for each calendar quarter during the royalty term contemplated by the Funding Agreement, in exchange for $100.0 million in cash. Specifically, the participation rate commences at 2.1 percent on annual global net sales of up to and equal to $1.5 billion, declining to 1.5 percent on annual global net sales exceeding $1.5 billion.

In addition, the Company had the option to repurchase 100% of the Revenue Participation Right from RPI for a purchase price of $155.0 million, if the Company entered into a definitive agreement to consummate a change of control. The Company did not exercise the Buy-Back Option which expired in July 2018.

***2018 License Agreement with AstraZeneca***

In September 2018, the Company entered into the 2018 AstraZeneca Agreement. Under the 2018 AstraZeneca Agreement, the Company paid AstraZeneca an upfront cash payment of $3,000 and 109,523 shares valued at $4,080 on the date of settlement, both of which are included in research and development expense, and is obligated to pay milestone payments to AstraZeneca totaling up to $55,000 upon the achievement of specified regulatory and commercial milestones and up to $50,000 upon the achievement of specified sales-based milestones. In addition, we will pay AstraZeneca tiered royalties ranging from high single-digit to low double-digits based on net sales of specified approved products, subject to specified reductions.

AstraZeneca granted Biohaven exclusive worldwide rights to develop and commercialize AZD3241, an oral myeloperoxidase ("MPO") inhibitor that AstraZeneca progressed through Phase 2 clinical trials. We plan to conduct a Phase 3 clinical trial of this product candidate, which will now be referred to as verdiperstat, for the treatment of multiple system atrophy ("MSA"), a rare, rapidly progressive and fatal neurodegenerative disease with no cure or effective treatments.

We are now solely responsible, and has agreed to use commercially reasonable efforts, for all development, regulatory and commercial activities related to verdiperstat. We may sublicense its rights under the Agreement and, if it does so, will be

(Amounts in thousands, except share and per share amounts)

**13. License and Other Agreements (Continued)**

obligated to pay a portion of any milestone payments received from the sublicensee to AstraZeneca in addition to any milestone payments we would otherwise be obligated to pay. We are also now responsible for the prosecution and maintenance of the patents related to verdiperstat and has the first right to prosecute infringement of the patents and defend challenges to the validity or enforceability of the patents.

The Agreement terminates on a country-by-country basis and product-by-product basis upon the expiration of the royalty term for such product in such country. Each royalty term begins on the date of the first commercial sale of the licensed product in the applicable country and ends on the later of 10 years from such first commercial sale or the expiration of the last to expire of the applicable patents in that country. The Agreement may be terminated earlier in specified situations, including termination for uncured material breach of the Agreement by either party, termination by AstraZeneca in specified circumstances, termination by us on a country-by-country basis with advance notice and termination upon a party's insolvency or bankruptcy.

***License Agreement with the University of Connecticut***

In October 2018, the Company announced it had signed an exclusive, worldwide option and license agreement (the "UConn Agreement") with the University of Connecticut ("UConn") for the development and commercialization rights to UC1MT, a therapeutic antibody targeting extracellular metallothionein. Under this agreement, we have the option to acquire an exclusive, worldwide license to UC1MT and its underlying patents to develop and commercialize throughout the world in all human indications. If the Company chooses to exercise the option, it would be obligated to pay UConn upon the achievement of specified regulatory and commercial milestones, and royalties of a low single-digit percentage of net sales of licensed products sold by the Company, its affiliates or its sublicensees.

**14. Income Taxes**

As a company incorporated in the British Virgin Islands ("BVI"), the Company is principally subject to taxation in the BVI. Under the current laws of the BVI, tax on a company's income is assessed at a zero percent tax rate. As a result, the Company has not recorded any income tax benefits from its losses incurred in the BVI during each reporting period, and no net operating loss carryforwards will be available to the Company for those losses. BVI has historically outsourced all of the research and clinical development for its programs under a master services agreement with BPI (see Note 18). As a result of providing services under this agreement, BPI was profitable during the years ended December 31, 2018 and 2017, and BPI is subject to taxation in the United States.

The Company's tax provision includes the effects of consolidating the results of operations of BPI, either as a variable interest entity for periods through the acquisition of BPI (see Note 18) or as of December 31, 2018 and 2017 as the Company's wholly owned subsidiary. Due to BPI's history of cumulative losses through September 30, 2016, the Company had recorded no tax benefits for the losses incurred by BPI through that date and had recorded a full valuation allowance against BPI's deferred tax assets, which consisted primarily of its U.S. net operating loss carryforwards for all periods through September 30, 2016. As of December 31, 2016, the Company fully utilized BPI's remaining U.S. net operating loss carryforwards and recorded a full release of the valuation allowance, which did not result in a material impact to the Company's income tax provision.

As of December 31, 2018, we evaluated our deferred tax assets and determined that a full valuation allowance on these assets was appropriate due to the generation of tax credits in excess of forecasted taxes. The Company recorded an income tax provision during the year ended December 31, 2018 of $467 which primarily represents certain state taxes for the period and federal taxes due to general business credit limitations.

Income (loss) before provision for income taxes consisted of the following:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| BVI | $ (246,829) | $ (130,359) | $ (63,677) |
| Foreign (U.S.) | 6,374 | 4,175 | 233 |
| Loss before provision for income taxes | $ (240,455) | $ (126,184) | $ (63,444) |

(Amounts in thousands, except share and per share amounts)

**14. Income Taxes (Continued)**

The provision for income taxes consisted of the following:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Current income tax provision: | | | |
| BVI | $ — | $ — | $ — |
| Foreign (U.S. federal and state) | 467 | 997 | 99 |
| Total current income tax provision | 467 | 997 | 99 |
| Deferred income tax provision (benefit): | | | |
| BVI | — | — | — |
| Foreign (U.S. federal and state) | — | 9 | (9) |
| Total deferred income tax provision (benefit) | — | 9 | (9) |
| Total provision for income taxes | $ 467 | $ 1,006 | $ 90 |

A reconciliation of the BVI statutory income tax rate of 0% to the Company's effective income tax rate is as follows:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| BVI statutory income tax rate | .0 % | .0 % | .0 % |
| Foreign tax rate differential | .6 | 1.2 | .1 |
| Tax Credits | (3.5) | (2.7) | .0 |
| Change in valuation allowance | 3.4 | 2.2 | .0 |
| Other | (.3) | .1 | .0 |
| Effective income tax rate | .2 % | .8 % | .1 % |

Net deferred tax assets (liabilities) consisted of the following:

| | December 31, | |
|---|---|---|
| | 2018 | 2017 |
| Deferred tax assets: | | |
| Foreign net operating loss carryforwards | $ — | $ — |
| Tax credits | 11,396 | 2,790 |
| Other | 1 | 1 |
| Total deferred tax assets | 11,397 | 2,791 |
| Deferred tax liabilities: | | |
| Other | (440) | (7) |
| Total deferred tax liabilities | (440) | (7) |
| Valuation allowance | (10,957) | (2,784) |
| Net deferred tax assets | $ — | $ — |

As of December 31, 2018 and 2017, the Company had no remaining foreign net operating loss carryforwards. The Company had federal and state research and development credits of $7,569 and $1,623 which begin to expire in 2037. As of December 31, 2018 the Company had federal orphan drug credits of $2,544 which can carryforward into 2038.

On December 22, 2017, the Tax Cuts and Jobs Act ("The Act"), was signed into law, resulting in significant changes to the Internal Revenue Code of 1986, as amended. These changes include a federal statutory rate reduction from 35% to 21%, limitation on the amount of research and development expenses deductible per year beginning in years after 2021, reduction of the Orphan Drug Credit from 50% to 25% of qualified clinical testing expenditures, increased limitations on certain executive

(Amounts in thousands, except share and per share amounts)

**14. Income Taxes (Continued)**

compensation, elimination of the Corporate Alternative Minimum Tax, and modifying or repealing other business deductions and credits. The revaluation of our deferred tax assets due to The Act was not material.

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2018 and 2017 were due primarily to generation of excess credits and were as follows:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Valuation allowance as of beginning of year | $ 2,784 | $ — | $ 16 |
| Decreases recorded as benefit to income tax provision | — | — | (16) |
| Increases recorded to income tax provision | 8,173 | 2,784 | — |
| Valuation allowance as of end of year | $ 10,957 | $ 2,784 | $ — |

The Company has not recorded any amounts for unrecognized tax benefits as of December 31, 2018 or 2017. The Company's policy is to record interest and penalties related to income taxes as part of its income tax provision. As of December 31, 2018 and 2017, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts had been recognized in the Company's statement of operations and comprehensive loss.

BPI files income tax returns in the U.S. and certain state jurisdictions. BPI's U.S. federal and state income tax returns are subject to tax examinations for the tax year ended December 31, 2015 and subsequent years. There are currently no income tax examinations pending.

**15. Net Loss per Share**

***Net Loss per Share***

Basic and diluted net loss per share attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd. was calculated as follows:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Numerator: | | | |
| Net loss | $ (240,922) | $ (127,190) | $ (63,534) |
| Net (income) loss attributable to non-controlling interests | — | — | 143 |
| Accretion of beneficial conversion feature on Series A preferred shares | — | (12,006) | — |
| Net loss attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd. | $ (240,922) | $ (139,196) | $ (63,677) |
| Denominator: | | | |
| Weighted average common shares outstanding—basic and diluted | 39,188,458 | 27,845,576 | 12,608,366 |
| Net loss per share attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd.—basic and diluted | $ (6.15) | $ (5.00) | $ (5.05) |

The Company's potential dilutive securities, which include stock options and warrants to purchase common shares, have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted average number of common shares outstanding used to calculate both basic and diluted net loss per share attributable to common shareholders is the same. The Company excluded the following potential common shares,

(Amounts in thousands, except share and per share amounts)

**15. Net Loss per Share (Continued)**

presented based on amounts outstanding at each period end, from the computation of diluted net loss per share attributable to common shareholders for the periods indicated because including them would have had an anti-dilutive effect:

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Options to purchase common shares | 7,444,179 | 6,151,643 | 3,864,425 |
| Warrants to purchase common shares | 221,751 | 821,751 | 600,000 |
| | 7,665,930 | 6,973,394 | 4,464,425 |

In addition to the potentially dilutive securities noted above, as of September 30, 2016, the Company agreed to issue warrants to purchase common shares to each of the Guarantor and Co-Guarantor of the Credit Agreement (see Note 9). In January 2017, the Company issued the warrants to the Guarantor and Co-Guarantor, pursuant to which each director received a warrant to purchase 107,500 common shares at an exercise price of $9.2911 per share. These warrants are included in the table above for the year ended December 31, 2017.

In January 2018, the anti-dilution price protection provisions contained within the warrants issued to each of the guarantor and co-guarantor of the Credit Agreement expired, and upon expiration of the provision, the Company discontinued classification of these warrants as a liability. As such, these warrants are excluded above for the year ended December 31, 2018.

The Company had also agreed under its agreements with AstraZeneca and BMS to issue common shares upon the achievement of specified milestones or upon the occurrence of specified events (see Notes 11 and 13). Because the necessary conditions for issuance of the shares had not been met as of December 31, 2016, the Company excluded these shares from the table above and from the calculation of diluted net loss per share for the year ended December 31, 2016. In May 2017, in connection with the completion of its IPO, the Company issued 538,149 common shares to AstraZeneca and 1,345,374 common shares to BMS in full satisfaction of its obligations to contingently issue equity securities pursuant to the license agreements. Accordingly, the table above does not include any shares related to the agreements with AstraZeneca and BMS for the year ended December 31, 2017.

**16. Commitments and Contingencies**

***Lease Agreement***

In December 2016, the Company entered into an assignment agreement to assume an operating lease for its office space in New Haven, Connecticut. The lease agreement expired in October 2018. In addition, the Company entered into a lease agreement for additional space which expired o n June 30, 2018. The Company recorded rent expense for these leases as follows:

| | Twelve Months Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Rent expense | $ 114 | $ 73 | $ — |

In August 2017, we entered into a lease agreement to consolidate our headquarters into a free standing building in New Haven, Connecticut, which we began occupying during the fourth quarter of 2018. The lease had a term of 85 months and commenced on January 1, 2018, with the ability to extend to 120 months. The Company had the option to purchase the property for $2,700 and executed that option in December 2018.

The Company recorded the following for the lease agreement for its new headquarters during the construction period:

| | Twelve Months Ended December 31, | | |
|---|---|---|---|
| | 2018 | 2017 | 2016 |
| Rent expense | $ 43 | $ 75 | $ — |
| Capitalized costs | 3,404 | 2,198 | — |

**16. Commitments and Contingencies (Continued)**

***License Agreements***

The Company has entered into license agreements with various parties under which it is obligated to make contingent and non-contingent payments (see Note 13). License agreements generally require the Company to pay annual maintenance fees and future payments upon the attainment of agreed upon development and/or commercial milestones. These agreements may also require minimum royalty payments based on sales of products developed from the applicable technologies, if any.

The Company has submitted an investigational new drug application ("IND") for BHV-3500, it's third generation CGRP receptor antagonist, and received approval to proceed and subsequently commenced a Phase 1 clinical trial in October of 2018 to permit later stage clinical trials. Per the BMS License Agreement, the Company is required to pay $2,000 to BMS on commencement of a Phase 1 clinical trial, and accordingly, the Company has recognized this liability in October of 2018. The payment obligation under the agreement is deferred until the earlier of the first approval or the discontinuation of the development of the Company's second generation CGRP receptor antagonist, rimegepant.

***Research Commitments***

The Company has entered into agreements with several CROs to provide services in connection with its preclinical studies and clinical trials. As of December 31, 2018, the Company had committed to minimum payments under these arrangements of $16,949, of which substantially all are due in the year ended December 31, 2019.

***Indemnification Agreements***

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. The Company's amended and restated memorandum and articles of association also provide for indemnification of directors and officers in specific circumstances. To date, the Company has not incurred any material costs as a result of such indemnification provisions. The Company does not believe that the outcome of any claims under indemnification arrangements will have a material effect on its financial position, results of operations or cash flows, and it has not accrued any liabilities related to such obligations in its consolidated financial statements as of December 31, 2018 or 2017.

***Legal Proceedings***

From time to time, in the ordinary course of business, the Company is subject to litigation and regulatory examinations as well as information gathering requests, inquiries and investigations. As of December 31, 2018, there were no matters which would have a material impact on the Company's financial results.

**17. Related Party Transactions**

***License Agreement with Yale***

On September 30, 2013, the Company entered into the Yale Agreement with Yale (see Note 13). Yale is a related party because the Company's Chief Executive Officer is one of the inventors of the patents that the Company has licensed from Yale and, as such, is entitled to a specified share of the glutamate product-related royalty revenues that may be received by Yale under the Yale Agreement. As partial consideration for the license under the Yale Agreement, on September 30, 2013, the Company issued to Yale 250,000 common shares, representing 5.1% of the Company's then outstanding equity on a fully diluted basis. The fair value of the shares, totaling $152, was recognized as research and development expense at the time of issuance of the shares. During the years ended December 31, 2018, 2017 and 2016, the Company recognized no material research and development expense under the Yale Agreement, and as of December 31, 2018 and 2017, the Company owed no amounts to Yale.

**17. Related Party Transactions (Continued)**

***Relationship with Yale University***

Dr. Coric, the Company's Chief Executive Officer, previously served as an associate clinical professor of psychiatry at Yale. While previously employed by Yale, Dr. Coric was a co-inventor of some of the patents that the Company licenses from Yale. Under Yale's policies, as a co-inventor, Dr. Coric is entitled to receive a share of any royalties that the Company pays to Yale under the agreement with respect to the covered intellectual property and any proceeds from Yale's sale of the common shares the Company issued to Yale in connection with the license agreement. During 2017, Yale sold the common shares and, pursuant to Yale's policies, Dr. Coric received a payment from Yale of $0.6 million in March 2018.

***Guarantor and Co-Guarantor Warrants***

The Guarantor and Co-Guarantor of the Credit Agreement with Wells Fargo are each shareholders and members of the board of directors of the Company. The Company issued warrants to the Guarantor and Co-Guarantor in exchange for their respective guaranties (see Notes 9). The warrants were issued on January 26, 2017, pursuant to which each director received a warrant to purchase 107,500 common shares at an exercise price of $9.2911 per share.

***Kleo Pharmaceuticals, Inc.***

The Company has an investment in the common stock of Kleo (see Note 5). Kleo is a related party because the Company has determined that it exercises significant influence over the operating and financial policies of Kleo. In connection with its investment in Kleo, the Company received the right to designate two members of Kleo's board of directors, who are the Chairman of the Company's board of directors and another director of the Company. Also, the President and controlling stockholder of Kleo is a shareholder of the Company. The Company completed the last of four scheduled tranche purchases in January 2018, consisting of 1,375,000 shares for cash consideration of $1,375. In November 2018, the Company participated in Kleo's Series B funding raise. The Company purchased 1,420,818 shares for cash consideration of $5,000. As of December 31, 2018, the Company owned 41.9% of Kleo's outstanding capital stock. The Company has also entered into a clinical development master services agreement with Kleo to assist Kleo with clinical development. As of December 31, 2018, the Company had not performed any services or received any payments under this agreement.

***Biohaven Pharmaceuticals, Inc.***

BPI is a related party because the three founders, each of whom beneficially owned one-third of the equity of BPI prior to the Company's acquisition of BPI on December 31, 2016 (see Note 18), are shareholders of the Company and also serve as the Company's Chairman of the board of directors, Chief Executive Officer and Chief Medical Officer, respectively. On December 31, 2016, the Company acquired 100% of the capital stock of BPI for aggregate purchase consideration of $595 in the form of promissory notes to each of the former stockholders of BPI. In connection with the closing of the Company's IPO in May 2017, the notes were paid in full, including principal of $595, and accrued interest of $9.

***AstraZeneca***

The Company entered into an exclusive license agreement with AstraZeneca in October 2016. As part of the consideration under the agreement and in connection with the completion of the Series A First Closing in October 2016 and the completion of the IPO in May 2017, AstraZeneca received shares of the Company's stock (see Notes 1, 11 and 13).

***Bristol Myers-Squibb Company***

The Company entered into an exclusive license agreement with BMS in July 2016. As part of the consideration under the agreement and in connection with the completion of the Company's IPO in May 2017, BMS received shares of the Company's stock (see Notes 1, 11 and 13). The Company recorded $2,000 and $5,000 of research and development expense related to a payment made during the years ended December 31, 2018 and 2017 for the achievement of a specified milestone.

**18. Acquisition of Biohaven Pharmaceuticals, Inc.**

The Company has historically outsourced all of the research and clinical development for its programs under a master services agreement (the "MSA") with BPI. The three founders of BPI, each of whom beneficially owned 33% of the equity of BPI prior to the Company's acquisition of BPI on December 31, 2016, are shareholders of the Company and also serve as the Company's Chairman of the board of directors, Chief Executive Officer, and Chief Medical Officer, respectively (see Note 17). BPI is a contract research organization whose only customer is the Company. Since its incorporation, substantially all of the

**18. Acquisition of Biohaven Pharmaceuticals, Inc (Continued)**

operations of BPI have been performed in service to the Company under the terms of the MSA, and substantially all of the funding for the operations of BPI was provided by the Company.

The Company determined that (i) it has the authority to direct the activities of BPI that most significantly impact the economics of the entity and (ii) the equity at risk in BPI is insufficient to finance its operations. As a result, the Company is deemed to have had a variable interest in BPI, and BPI is deemed to be a variable interest entity ("VIE") of which the Company is the primary beneficiary. Since the date of the Company's incorporation in September 2013, the Company has consolidated the results of BPI. Upon original consolidation, the Company applied purchase accounting by recording the fair values of BPI's assets acquired and liabilities assumed, which were determined to be zero because BPI had not yet commenced any operations. For the year ended December 31, 2016, 100% of the equity in BPI was reflected as a net loss attributable to non-controlling interest on the consolidated statement of operations and comprehensive loss.

On December 31, 2016, the Company entered into stock purchase agreements with each of the stockholders of BPI, acquiring 100% of the issued and outstanding shares of BPI for aggregate purchase consideration of $595, and as a result, for periods subsequent to the acquisition, the Company no longer reports any non-controlling interest related to BPI.

The Company funded the acquisition through the issuance of promissory notes to each of the former stockholders of BPI. In May 2017, in connection with the completion of the IPO, the notes became immediately due and payable, and the Company paid the notes, including principal and unpaid interest, in full.

Because the Company consolidated BPI as a VIE prior to the acquisition, the acquisition of all of the capital stock of BPI did not result in a change of control for accounting purposes and was accounted for as an equity transaction. Accordingly, as of the acquisition date, the $86 carrying value of the non-controlling interest on December 31, 2016 was derecognized and the difference between the carrying value of the non-controlling interest of $86 and the purchase price of $595 was recorded as a $509 reduction to additional paid-in capital. There were no changes to this accounting treatment of BPI during the years ended December 31, 2018 and 2017.

For the year ended December 31, 2016 when the Company consolidated BPI as a VIE, the Company recorded net income of $143 attributable to non-controlling interests.

(Amounts in thousands, except share and per share amounts)

**19. Quarterly Financial Data (Unaudited)**

The following information has been derived from unaudited consolidated financial statements that, in the opinion of management, include all recurring adjustments necessary for a fair statement of such information.

| | Three Months Ended | | | |
|---|---|---|---|---|
| | March 31, 2018 | June 30, 2018 | September 30, 2018 | December 31, 2018 |
| Operating expenses: | | | | |
| Research and development | $ 75,579 | $ 29,052 | $ 47,362 | $ 37,958 |
| General and administrative | 7,857 | 9,064 | 7,574 | 10,108 |
| Total operating expenses | 83,436 | 38,116 | 54,936 | 48,066 |
| Loss from operations | (83,436) | (38,116) | (54,936) | (48,066) |
| Other income (expense): | | | | |
| Interest expense | (8) | (13) | (12) | (5) |
| Non-cash interest expense on liability related to sale of future royalties | — | (501) | (5,633) | (5,592) |
| Change in fair value of warrant liability | (1,182) | — | — | — |
| Loss from equity method investment | (728) | (641) | (697) | (742) |
| Other | (21) | 27 | (2) | (151) |
| Total other income (expense), net | (1,939) | (1,128) | (6,344) | (6,490) |
| Loss before provision for income taxes | (85,375) | (39,244) | (61,280) | (54,556) |
| Provision for income taxes | 87 | 25 | 161 | 194 |
| Net loss attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd. | $ (85,462) | $ (39,269) | $ (61,441) | $ (54,750) |
| Net loss per share attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd.—basic and diluted | $ (2.32) | $ (1.01) | $ (1.53) | $ (1.34) |
| Weighted average common shares outstanding—basic and diluted | 36,793,090 | 38,942,545 | 40,147,735 | 40,938,709 |

(Amounts in thousands, except share and per share amounts)

**19. Quarterly Financial Data (Unaudited)(Continued)**

| | Three Months Ended | | | |
|---|---|---|---|---|
| | March 31, 2017 | June 30, 2017 | September 30, 2017 | December 31, 2017 |
| Operating expenses: | | | | |
| Research and development | $ 10,740 | $ 21,019 | $ 34,996 | $ 22,686 |
| General and administrative | 3,757 | 4,199 | 4,571 | 5,614 |
| Total operating expenses | 14,497 | 25,218 | 39,567 | 28,300 |
| Loss from operations | (14,497) | (25,218) | (39,567) | (28,300) |
| Other income (expense): | | | | |
| Interest expense | (305) | (362) | (239) | — |
| Interest income | — | — | 10 | (10) |
| Change in fair value of warrant liability | (454) | (2,629) | (2,426) | 2,268 |
| Change in fair value of derivative liability | 289 | 223 | — | — |
| Change in fair value of contingent equity liability | (3,375) | (9,707) | — | — |
| Loss from equity method investment | (218) | (348) | (638) | (681) |
| Total other income (expense), net | (4,063) | (12,823) | (3,293) | 1,577 |
| Loss before provision for income taxes | (18,560) | (38,041) | (42,860) | (26,723) |
| Provision for income taxes | 193 | 399 | 55 | 359 |
| Net loss and comprehensive loss | $ (18,753) | $ (38,440) | $ (42,915) | $ (27,082) |
| Accretion of beneficial conversion feature on Series A preferred shares | (4,000) | (8,006) | — | — |
| Net loss attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd. | $ (22,753) | $ (46,446) | $ (42,915) | $ (27,082) |
| Net loss per share attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd.—basic and diluted | $ (1.74) | $ (1.78) | $ (1.19) | $ (0.75) |
| Weighted average common shares outstanding—basic and diluted | 13,088,861 | 26,038,192 | 35,930,698 | 35,984,111 |

During the quarter ended December 31, 2017, the Company recorded a $3,294 out-of-period adjustment to increase non-cash share-based compensation expense. Management has concluded that the error is not material to the current or prior period financial statements.

**Exhibit 21.1**

**SUBSIDIARIES OF BIOHAVEN PHARMACEUTICAL HOLDING COMPANY LTD.**

| Name | Jurisdiction of Incorporation |
|---|---|
| Biohaven Pharmaceuticals, Inc. | Delaware |
| Biohaven Asia Pacific Ltd. | British Virgin Islands |
| BioShin Hong Kong Limited | Hong Kong |
| Biohaven Therapeutics Ltd. | British Virgin Islands |

**Exhibit 23.1**

**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We hereby consent to the incorporation by reference in the Registration Statement on Form S-8 (No. 333-225224 and 333-218193) of Biohaven Pharmaceutical Holding Company Ltd. of our report dated February 28, 2019 relating to the financial statements and the effectiveness of internal control over financial reporting, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP

Hartford, Connecticut
February 28, 2019

**Exhibit 31.1**

**CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER**
**PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Vlad Coric, certify that:

1. I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2018 of Biohaven Pharmaceutical Holding Company Ltd. (the "registrant");

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 28, 2019

/s/ VLAD CORIC, M.D.

Vlad Coric, M.D.
*Chief Executive Officer*
*(principal executive officer)*

**Exhibit 31.2**

**CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER**
**PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, James Engelhart, certify that:

1. I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2018 of Biohaven Pharmaceutical Holding Company Ltd. (the "registrant");

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 28, 2019

/s/ JAMES ENGELHART

James Engelhart
*Chief Financial Officer*
*(principal financial officer)*

**Exhibit 32.1**

**CERTIFICATIONS OF**
**PRINCIPAL EXECUTIVE OFFICER AND PRINCIPAL FINANCIAL OFFICER**
**PURSUANT TO 18 U.S.C. SECTION 1350,**
**AS ADOPTED PURSUANT TO**
**SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Vlad Coric, M.D., Chief Executive Officer of Biohaven Pharmaceutical Holding Company Ltd. (the "Company"), and James Engelhart, Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

1. The Company's Annual Report on Form 10-K for the year ended December 31, 2018, to which this Certification is attached as Exhibit 32.1 (the "Periodic Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

**IN WITNESS WHEREOF**, the undersigned have set their hands hereto as of the 28 day of February, 2019.

| | |
|---|---|
| /s/ VLAD CORIC, M.D. | /s/ JAMES ENGELHART |
| Vlad Coric, M.D. | James Engelhart |
| *Chief Executive Officer* | *Chief Financial Officer* |
| *(principal executive officer)* | *(principal financial officer)* |

*This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Exchange Act (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.