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Filed Pursuant to Rule 424(b)(4) Registration No. 333-217214

PROSPECTUS

### *9,900,000 Shares*



**COMMON SHARES** 

Biohaven Pharmaceutical Holding Company Ltd. is offering 9,900,000 of its common shares. This is our initial public offering, and no public market currently exists for our common shares.

Our common shares have been approved for listing on the New York Stock Exchange under the symbol "BHVN."

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012 and, as such, have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings. See "Prospectus Summary—Implications of Being an Emerging Growth Company."

Investing in our common shares involves risks. Please see "Risk Factors" beginning on page 14.

#### PRICE \$17.00 A SHARE

Per Share Total	Price to Public \$17.00 \$168,300,000	Underwriting Discounts and <u>Commissions<sup>(1)</sup></u> \$1.19 \$11,781,000	Proceeds, Before Expenses, to Biohaven \$15.81 \$156,519,000
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(1) We have agreed to reimburse the underwriters for certain expenses in connection with this offering. See "Underwriting" in this prospectus for a description of compensation payable to the underwriters.

We have granted the underwriters an option to purchase up to 1,485,000 additional common shares at the initial public offering price less the underwriting discount. The underwriters can exercise this option at any time within 30 days after the date of this prospectus.

Certain of our existing principal shareholders, directors and their affiliated entities, including Aisling Capital, RA Capital Management, Venrock and Vivo Capital, have agreed to purchase an aggregate of 3,142,117 common shares in this offering at the initial public offering price per share. The underwriters will receive the same underwriting discount on the shares purchased by these entities as they will on the other shares sold to the public in this offering.

The underwriters expect to deliver the common shares to purchasers on or about May 9, 2017.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

MORGAN STANLEY

PIPER JAFFRAY

BARCLAYS

WILLIAM BLAIR

NEEDHAM & COMPANY

May 3, 2017

DACE

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Neither we nor the underwriters have authorized anyone to provide any information or to make any representations other than those contained in this prospectus or in any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus or in any applicable free writing prospectus is current only as of its date, regardless of its time of delivery or any sale of our common shares. Our business, financial condition, results of operations, and prospects may have changed since that date.

Through and including May 28, 2017 (25 days after the date of this prospectus), all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

For investors outside the United States: neither we nor the underwriters have done anything that would permit this offering or possession or distribution of this prospectus or any free writing prospectus we may provide to you in connection with this offering in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus and any such free writing prospectus outside of the United States.

#### **PROSPECTUS SUMMARY**

This summary highlights information contained in greater detail elsewhere in this prospectus. This summary is not complete and does not contain all of the information you should consider in making your investment decision. You should read the entire prospectus carefully before making an investment in our common shares. You should carefully consider, among other things, our financial statements and the related notes and the sections titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included elsewhere in this prospectus. Unless the context otherwise requires, we use the terms "Biohaven," "company," "we," "us" and "our" in this prospectus to refer to Biohaven Pharmaceutical Holding Company Ltd. and, where appropriate, our subsidiaries.

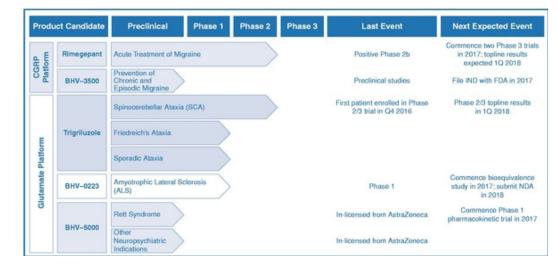
#### Overview

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 two distinct mechanistic platforms—calcitonin gene-related peptide, or CGRP, receptor antagonists and glutamate modulators—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 markets and orphan indications. The most advanced product candidate from our CGRP receptor antagonist platform is rimegepant, which we are developing for the acute treatment of migraine and for which we intend to initiate two Phase 3 clinical trials in the second half of 2017, with topline results expected in the first quarter of 2018. The most advanced product candidate from our glutamate modulation platform is trigriluzole, which we are developing for the treatment of ataxias with an initial focus on spinocerebellar ataxia, or SCA. We have received orphan drug designation from the U.S. Food and Drug Administration, or FDA, for trigriluzole in SCA, and we began a Phase 2/3 clinical trial in SCA in December 2016 and expect to report topline results in the first quarter of 2018. Our second most advanced product candidate from our glutamate modulation platform is BHV-0223, which we are developing for the treatment of amyotrophic lateral sclerosis, or ALS, a neurodegenerative disease that affects nerve cells in the brain and spinal cord. We have received orphan drug designation from the FDA for BHV-0223 in ALS.

We believe many of our product candidates have the potential to be first-in-class or best-in-class treatment options, while others will potentially represent the first available treatment options for their indications. Based on the data from its Phase 2b clinical trial, we believe rimegepant has the potential to be the best-in-class CGRP receptor antagonist for the acute treatment of migraine, having shown statistically significant improvement on the symptoms of pain, nausea, photophobia and phonophobia associated with migraine attacks. To our knowledge, rimegepant is the only small molecule CGRP receptor antagonist currently in development for the acute treatment of migraine to have achieved statistical significance, meaning there is a low probability, typically less than 5%, that the difference happened by chance, on all of these efficacy measures in a single study. We also believe that trigriluzole has the potential to be the first FDA-approved drug treatment option for ataxias. We intend to expedite development of trigriluzole for SCA using the Section 505(b)(2) regulatory pathway and are currently conducting a Phase 2/3 trial that we believe, if successful, may be sufficient to support our application for regulatory approval of trigriluzole. We believe that BHV-0223 has the potential to be the first-in-class sublingual treatment for ALS. BHV-0223 is designed to deliver the unique pharmacologic, glutamate modulation effects of riluzole, which has shown a survival benefit for ALS patients, and which is currently the only treatment for ALS approved by the FDA. We believe BHV-0223 could also provide best-in-class formulation attributes, such as ease of administration, more predictable pharmacokinetic performance, no food effect, reduced drug load and reduced liver exposure.

#### **Product Candidates**

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



Our CGRP Receptor Antagonist Platform: Rimegepant and BHV-3500 Targeting Migraine

Our CGRP receptor antagonist platform comprises two product candidates: rimegepant for the acute treatment of migraine and BHV-3500 for the prevention of chronic and episodic migraine. Rimegepant, the lead product candidate, is an orally available, selective and potent small molecule CGRP receptor antagonist. 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 2010 rates migraine as the seventh highest specific cause of disability worldwide. According to the American Migraine Foundation, migraine affects approximately 36 million people in the United States, and treatment of migraine accounted for an estimated market of approximately \$1.9 billion in 2012 in the United States. Current treatment approaches, such as triptans, can be limited by headache recurrence, which are headaches that are relieved and then reoccur within 24 hours after taking migraine medication, and cardiovascular contraindications or warnings. We believe rimegepant has the potential to be a best-in-class CGRP receptor antagonist for the acute treatment of migraine with the ability to address important unmet needs, such as durable efficacy across all four traditional migraine symptoms and reduced incidence of headache recurrence, without contraindications or warnings in patients with cardiovascular disease or hypertension, since its CGRP-based mechanism of action does not involve active vasoconstriction, or the constriction of blood vessels.

In a Phase 2b, double-blind, randomized, placebo-controlled, dose-ranging clinical trial of 812 patients completed by Bristol-Myers Squibb Company, or BMS, rimegepant dosed at 75 mg was observed to have statistically significant improvement as compared to placebo on all four key migraine symptoms—pain, nausea, photophobia and phonophobia—the four traditional endpoints identified by the FDA for drug approval. To our knowledge based on publicly available information, rimegepant is the only small molecule CGRP receptor antagonist currently in development for the acute treatment of migraine that has achieved statistically significant improvement on all four of the traditional endpoints within a single study. As of December 31, 2016, approximately 687 subjects have received single or multiple doses of rimegepant, no treatment-related serious adverse events have been observed and adverse events have generally been mild and transient in nature. In the second half of 2017, we plan to commence two Phase 3 clinical trials of rimegepant for the acute treatment of migraine, with topline results expected in the first quarter of 2018. We are advancing the 75 mg dose of rimegepant in our Phase 3 clinical trials, as that dose was the lowest

dose in the Phase 2b trial at which statistically significant improvements as compared to placebo were observed in the four key migraine symptoms, and there did not appear to be additional benefits of higher doses, which is a general characteristic of the dose-response profile of acute treatments for migraine.

Based on the results from the Phase 2b trial and earlier-stage development, we believe rimegepant offers the following clinical and product benefits for the acute treatment of migraine:

- **Oral Availability.** To our knowledge, rimegepant is one of only two orally available small molecule CGRP receptor antagonists that are currently in late-stage clinical development for the acute treatment of migraine.
- **Comprehensive Treatment Effect.** In the Phase 2b trial, the 75 mg dose of rimegepant showed statistically significant improvement as compared to placebo across all four key migraine symptoms: pain, nausea, photophobia and phonophobia. To our knowledge based on publicly available information, rimegepant is the only small molecule CGRP receptor antagonist currently in development that has achieved statistically significant improvement on all four of these key migraine symptoms within a single study.
- **Durable Improvement.** In the Phase 2b trial, the 75 mg dose of rimegepant showed statistically significant improvement as compared to placebo on pain freedom at two-to-24 hours and two-to-48 hours after dosing, and on pain relief at two and 24 hours after dosing, showing durability of treatment effect.
- **Favorable Safety Profile.** In the Phase 2b trial, rimegepant was generally well tolerated with low rates of adverse events, or AEs, no discontinuations for AEs, no treatment-related serious adverse events and no deaths.
- Low Risk of Cardiovascular Side Effects. Preclinical and clinical evidence suggests that CGRP receptor antagonists, such as rimegepant, have an absence of vasoconstrictor activity and lack 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.

BHV-3500, the second product candidate from our CGRP receptor antagonist platform, is a small molecule, structurally distinct from rimegepant, that we are developing for the prevention of chronic and episodic migraine. BHV-3500 is potent, highly soluble and selective at the human CGRP receptor. In addition, BHV-3500 has demonstrated in nonclinical studies characteristics that we believe will make it particularly well suited for daily preventative treatment of chronic and episodic migraine. In 2017, we plan to commence studies to enable an investigational new drug application, or IND, to ultimately pursue clinical trials of BHV-3500 for the prevention of chronic and episodic migraine.

#### Our Glutamate Modulation Platform: Trigriluzole, BHV-0223 and BHV-5000 Targeting Orphan Neurological Indications

Under our glutamate modulation platform, we are currently developing three product candidates, trigriluzole (previously known as BHV-4157) for the treatment of ataxias, BHV-0223 for the treatment of ALS and BHV-5000 for the treatment of symptoms associated with Rett syndrome, including breathing irregularities. These product candidates modulate the glutamate system via two distinct mechanisms—glutamate transporter modulation (trigriluzole and BHV-0223) and glutamate *N*-methyl-D-aspartate, or NMDA, receptor antagonism (BHV-5000).

Trigriluzole is a third-generation tripeptide prodrug that converts to the active metabolite riluzole that we are developing for the treatment of ataxias. We believe that trigriluzole will qualify as a new chemical entity, or NCE, if it receives regulatory approval by the FDA. Trigriluzole has the potential to be the first

drug approved by the FDA for the treatment of ataxias, and we have chosen spinocerebellar ataxia, or SCA, as our lead indication. SCA is one of a group of rare genetic disorders that is characterized by slowly progressive incoordination of gait, speech and hand and eye movements. In general, a person with SCA retains full mental capacity but progressively loses physical control over voluntary muscles. 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. Other ataxias affect an aggregate of greater than 100,000 individuals in the United States. No approved drug treatments for SCA are currently available. We believe that trigriluzole may be effective in the treatment of SCA based on the results of two prior randomized controlled trials conducted by third parties, in which riluzole was observed to have statistically significant improvements in ataxia-related endpoints, and the results of multiple in vivo and in vitro preclinical studies that suggest that trigriluzole may mitigate the limitations of riluzole. As of December 31, 2016, trigriluzole had been dosed in 58 subjects in a Phase 1 clinical trial and has been generally well tolerated, without evidence of novel, clinically significant safety signals or lab abnormalities compared to the active metabolite riluzole. In May 2016, we received orphan drug designation from the FDA for trigriluzole in SCA, and we intend to develop trigriluzole for SCA under Section 505(b)(2) of the U.S. Federal Food, Drug, and Cosmetic Act. We believe our Phase 2/3 clinical trial, which 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, if successful, may be sufficient to support our application for regulatory approval of trigriluzole. The primary outcome measure of our Phase 2/3 clinical trial is the change from baseline in a patient's score on the Scale for the Assessment and Rating of Ataxia, or SARA, which is a validated scale that has been used in a third-party clinical trial for the treatment of hereditary ataxias (including SCA), after eight weeks of treatment. We enrolled the first patient in our Phase 2/3 clinical trial in December 2016, and we expect to report topline results from this trial in the first quarter of 2018. If the results of this trial are positive, we anticipate submitting a new drug application, or NDA, to the FDA in 2018.

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

- **Improved Bioavailability.** Trigriluzole 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.
- **No Negative Food Effect.** Trigriluzole shows no food effect in human studies, meaning that the drug will not be associated with special meal restrictions.
- **Lower Overall Drug Burden to the Liver.** As a prodrug that mitigates first-pass liver metabolism, 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. We believe these attributes of trigriluzole will reduce the potential for adverse liver effects.
- **Optimized Dosing Regimen and Compliance.** Trigriluzole has been developed as a convenient once-daily dose, which could improve patient compliance. We believe these are important features to optimize long-term health outcomes.
- **Potential for Developing Multiple Formulations.** Trigriluzole is highly soluble and does not exhibit the oral numbness associated with riluzole tablets. As such, we believe trigriluzole has the potential to be developed in multiple formulations, including intranasal, subcutaneous, intravenous, sublingual and other forms.

BHV-0223 is a sublingual, oral disintegrating tablet, or ODT, formulation of riluzole that we are developing for the treatment of ALS. ALS is a progressive neurodegenerative motor neuron disease that affects nerve cells in the brain and the spinal cord. 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. Orally administered riluzole, which was approved by the FDA in 1995, remains the only agent shown to extend survival and time to tracheostomy in patients with ALS, although it has significant shortcomings that limit its utility. We believe that BHV-0223 has the potential to significantly improve the treatment of patients with ALS by combining the unique pharmacologic activities of glutamate modulation that are conferred by riluzole with an improved pharmacologic profile that results in easier administration, more predictable pharmacokinetic performance, no food effect, reduced drug load and reduced liver exposure compared to oral riluzole. As of January 31, 2017, BHV-0223 had been dosed in 11 subjects. No treatment-related serious adverse events have been observed and adverse events have generally been mild and transient in nature. In December 2016, we received orphan drug designation from the FDA for BHV-0223 in ALS. In 2017, we plan to commence a bioequivalence study of BHV-0223 40 mg to riluzole 50 mg in healthy volunteers. We plan to subsequently submit an NDA for the use of BHV-0223 in patients with ALS and pursue regulatory approval under the Section 505(b)(2) regulatory pathway.

BHV-5000 is an orally available, first-in-class, low-trapping, NMDA receptor antagonist prodrug of the intravenous drug lanicemine that we are developing for the treatment of symptoms associated with Rett syndrome, including breathing irregularities. 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. We are studying BHV-5000 in Rett syndrome based on results of ketamine studies in preclinical mouse models that have shown improvement in key clinical features of the disease, including 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 show clinical improvements. As of December 31, 2016, BHV-5000 had been dosed in approximately 40 healthy subjects in a Phase 1 clinical trial conducted by AstraZeneca AB, or AstraZeneca, and has been observed to be well tolerated with no clinically relevant safety signals. BHV-5000's active metabolite, lanicemine, has been administered to approximately 790 subjects in clinical trials conducted by AstraZeneca, in single or multiple doses, and has been observed to be generally well tolerated with most adverse events being mild and transient in nature. We are in the process of developing a commercial formulation of BHV-5000 with acceptable shelf-life and stability at room temperature. After a confirmatory Phase I trial, which we plan to commence in 2017, to bridge pharmacokinetics with a prior formulation, we plan to commence a single Phase 2/3 clinical trial of BHV-5000 for the treatment of breathing irregularities associated with Rett syndrome in 2018 which, if successful, we believe may be sufficient to support our application for regulatory approval.

#### **Our Strategy**

Our goal is to become a leader in the development of innovative therapies for neurological diseases that have the potential to change current treatment paradigms. The key elements of our strategy to achieve this goal include:

• **Rapidly advance and commercialize our portfolio of migraine product candidates.** In the second half of 2017, we expect to initiate two Phase 3 clinical trials with rimegepant for the acute treatment of migraine, with topline results expected in the first quarter of 2018. We are also planning a 12-month, long-term safety study of rimegepant to meet FDA requirements for approval. We are designing our Phase 3 development program to support regulatory approval in the United States, as well as to support regulatory filings in Europe and Japan.

- Complete the development and commercialization of our novel glutamate modulator trigriluzole as potentially the first FDA-approved drug treatment for patients suffering from ataxias. We anticipate receiving topline results of our Phase 2/3 clinical trial of trigriluzole in SCA in the first quarter of 2018 and, if positive, submitting an NDA in 2018. We designed our Phase 2/3 clinical trial to support regulatory approval in the United States as well as to support regulatory filings in Europe and Japan.
- Demonstrate bioequivalence and prepare for commercialization of our low-dose, oral disintegrating sublingual product candidate, BHV-0223, for ALS patients. We plan to launch a study to compare the bioequivalence of our sublingually absorbed ODT formulation of riluzole, BHV-0223, to orally delivered riluzole tablets and subsequently submit an NDA in 2018.
- Advance BHV-5000 into clinical trials to assess its potential to be the first approved treatment for patients suffering from breathing irregularities associated with Rett syndrome. After a confirmatory Phase 1 clinical trial to bridge pharmacokinetics with the prior formulation, we plan to initiate a Phase 2/3 clinical trial in Rett syndrome in 2018.
- Maximize the therapeutic and commercial potential of our existing product candidates by exploring their use for multiple indications. Based on the broad mechanistic potential of our glutamate modulation platform, we believe that our product candidates may have utility in a wide array of conditions. We plan to explore the use of our product candidates in additional therapeutic indications where glutamate plays a central role in the pathophysiology of disease, including anxiety and mood disorders.
- Actively manage our product portfolio and opportunistically enter into strategic collaborations. We plan to retain our worldwide commercialization rights for some of our key product candidates while for other product candidates we will consider partnership opportunities to maximize returns. Leveraging our management team's deep large pharma relationships and experience will be a key component of this strategy.

#### **Our Team**

We are led by a team of experienced executives who have held senior research and development positions at leading biotech and large pharmaceutical companies. Members of our management team and board of directors have deep experience leading neuroscience research and have been involved in the development and commercialization of numerous drugs, such as Zoloft, Abilify, Opdivo, Yervoy and Soliris. This depth of experience has facilitated our ability to license important product candidates and intellectual property from top-tier pharmaceutical companies and leading academic institutions, such as AstraZeneca, BMS, ALS Biopharma, Rutgers University, the Massachusetts General Hospital (a teaching hospital of Harvard Medical School) and Yale University. Members of our Scientific Advisory Board hold or have held affiliations with Yale University, Harvard Medical School, the National Institutes of Health and the FDA. We also have ongoing academic collaborations with Johns Hopkins University, Columbia University, Rutgers University and Yale University. We believe the strength of our management team and board of directors positions us well to enter into additional license and collaboration arrangements with world-class institutions.

#### **Risks Associated with Our Business**

Our business is subject to a number of risks of which you should be aware before making a decision to invest in our common shares. These risks are discussed more fully in the "Risk Factors" section of this prospectus. These risks include the following:

- 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.
- 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.
- 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 rely in part 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 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 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 currently have no 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.
- If we are unable to obtain and maintain patent protection for our technology and product candidates, or if the scope of the patent protection obtained is not sufficiently broad, we may not be able to compete effectively in our markets.
- 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.
- There has been no public market for our common shares prior to this offering, and an active market in the shares may not develop or be liquid enough for investors to resell our common shares quickly or at the market price.
- We are an "emerging growth company," and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies will make our common shares less attractive to investors.
- You may have fewer protections as a shareholder of our company, as the rights of shareholders under British Virgin Islands law differ from those under U.S. law.
- Our independent registered public accounting firm has included an explanatory paragraph relating to our ability to continue as a going concern in its report on our audited financial statements included in this prospectus.

• We have identified material weaknesses in our internal control over financial reporting. If we are unable to remediate these material weaknesses, or if we experience additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect investor confidence in us and, as a result, the value of our common shares.

#### **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 234 Church Street, New Haven, Connecticut 06510 and our telephone number is (203) 404-0410. Our website address is *www.biohavenpharma.com*. The information contained on our website is not incorporated by reference into this prospectus, and you should not consider any information contained on, or that can be accessed through, our website as part of this prospectus or in deciding whether to purchase our common shares.

We have three wholly owned subsidiaries, including Biohaven Pharmaceuticals, Inc., a Delaware corporation. Following this offering, we expect to form an additional subsidiary that will be incorporated under the laws of Ireland. We expect that this Irish subsidiary 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. As a result, we expect that we will become subject to taxation in Ireland in the future.

We have proprietary rights to a number of trademarks used in this prospectus which are important to our business, including the Biohaven logo. Solely for convenience, the trademarks and trade names in this prospectus are referred to without the  $\mathbb{R}$  and  $^{TM}$  symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. All other trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners.

#### **Implications of Being an Emerging Growth Company**

As a company with less than \$1.07 billion in revenues during our last fiscal year, we qualify as an emerging growth company as defined in the Jumpstart Our Business Startups Act, or the JOBS Act, enacted in 2012. As an emerging growth company, we expect to take advantage of reduced reporting requirements that are otherwise applicable to public companies. These provisions include, but are not limited to:

- being permitted to present only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure in this prospectus;
- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended;
- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We may use these provisions until the last day of our fiscal year following the fifth anniversary of the completion of this offering. However, if certain events occur prior to the end of such five-year period,

including if we become a "large accelerated filer," our annual gross revenues exceed \$1.07 billion or we issue more than \$1.0 billion of non-convertible debt in any three-year period, we will cease to be an emerging growth company prior to the end of such five-year period.

We have elected to take advantage of certain of the reduced disclosure obligations in the registration statement of which this prospectus is a part and may elect to take advantage of other reduced reporting requirements in future filings. As a result, the information that we provide to our shareholders may be different than you might receive from other public reporting companies in which you hold equity interests.

The JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. We have irrevocably elected not to avail ourselves of this exemption and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

	THE OFFERING
Common shares offered	9,900,000 shares
Common shares outstanding after this offering	34,230,583 shares (35,715,583 shares if the underwriters exercise their over-allotment option in full)
Over-allotment option	We have granted the underwriters the option, exercisable for 30 days from the date of this prospectus, to purchase up to 1,485,000 additional common shares.
Use of proceeds	We expect the net proceeds from this offering to be approximately \$152.9 million, based on the initial public offering price of \$17.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.
	We anticipate that the net proceeds from this offering, together with our existing cash, will be used to advance our CGRP receptor antagonist and glutamate modulation platform product candidates; to repay indebtedness under our credit agreement and notes payable to related parties; to satisfy our obligation to purchase shares of capital stock of a privately held preclinical-stage company; and for working capital and other corporate purposes, including satisfaction of any of our milestone payment obligations under our license agreements. See "Use of Proceeds" on page 78 for additional information.
Directed share program	At our request, the underwriters have reserved for sale at the initial public offering price per share up to 495,000 common shares, or 5% of the common shares offered by this prospectus, to certain individuals through a directed share program, including employees, directors and other persons associated with us. If purchased by these persons, these shares will not be subject to a lock-up restriction, except in the case of shares purchased by any director or officer, which will be subject to a 180-day lock-up restriction. The number of common shares available for sale to the general public will be reduced by the number of reserved shares sold to these individuals. Any reserved shares not purchased by these individuals will be offered by the underwriters to the general public on the same basis as the other common shares offered under this prospectus. See "Underwriting."
Risk factors	See "Risk Factors" beginning on page 14 and the other information included in this prospectus for a discussion of factors you should consider carefully before deciding to invest in our common shares.
NYSE symbol	BHVN

1,883,523 common shares to BMS and AstraZeneca in connection with this offering pursuant to our license agreements with BMS and AstraZeneca, and excludes:

- 4,335,344 common shares issuable upon the exercise of stock options outstanding as of February 28, 2017, at a weighted average exercise price of \$4.23 per share;
- 815,000 common shares issuable upon the exercise of warrants outstanding as of February 28, 2017, at a weighted average exercise price of \$6.57 per share;
- 563,886 common shares reserved for future issuance under our 2014 Equity Incentive Plan, as amended, or the 2014 Plan, as of February 28, 2017 (of which options to purchase an aggregate of 563,514 common shares were issued subsequent to February 28, 2017, at a weighted average exercise price of \$10.80 per share); and
- 2,712,741 common shares reserved for future issuance under our 2017 Equity Incentive Plan, or the 2017 Plan, and 339,139 common shares reserved for future issuance under our 2017 Employee Share Purchase Plan, or ESPP, each of which became effective upon the signing of the underwriting agreement related to this offering, as well as any automatic increases in the number of common shares reserved for future issuance under the 2017 Plan and the ESPP.

Except as otherwise indicated herein, all information in this prospectus, including the number of shares that will be outstanding after this offering, assumes or gives effect to:

- the conversion of all outstanding Series A preferred shares into an aggregate of 9,358,560 common shares upon the closing of this offering;
- the issuance of an aggregate of 1,883,523 common shares to BMS and AstraZeneca in connection with this offering pursuant to our license agreements with BMS and AstraZeneca;
- no exercise of the outstanding options and warrants described above; and
- no exercise of the underwriters' over-allotment option.

Certain of our existing principal shareholders, directors and their affiliated entities have agreed to purchase an aggregate of 3,142,117 common shares in this offering at the initial public offering price per share. The underwriters will receive the same underwriting discount on the shares purchased by these entities as they will on the other shares sold to the public in this offering.

#### SUMMARY CONSOLIDATED FINANCIAL DATA

You should read the following summary consolidated financial data together with our consolidated financial statements and the related notes appearing at the end of this prospectus and the "Selected Consolidated Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of this prospectus. We have derived the consolidated statement of operations data for the years ended December 31, 2015 and 2016 and the consolidated balance sheet data as of December 31, 2016 from our audited consolidated financial statements appearing at the end of this prospectus. Our historical results are not necessarily indicative of results that may be expected in any future period.

	Year Ended December 31,			
		2015		2016
			sands, except are data)	
Consolidated Statement of Operations Data:		per sna	. c u	
Operating expenses:				
Research and development	\$	7,559	\$	55,52
General and administrative		2,137		5,10
Total operating expenses		9,696		60,63
Loss from operations		(9,696)		(60,63
Other income (expense), net		(370)		(2,80
Loss before provision for income taxes		(10,066)		(63,44
Provision for income taxes				9
Net loss		(10,066)		(63,53
Less: Net income (loss) attributable to non-controlling interests		(4)		14
Net loss attributable to common shareholders of Biohaven Pharmaceutical Holding				
Company Ltd.	\$	(10,062)	\$	(63,67
Net loss per share attributable to common shareholders of Biohaven Pharmaceutical				
Holding Company Ltd.—basic and diluted <sup>(1)</sup>	\$	(0.91)	\$	(5.0
Weighted average common shares outstanding—basic and diluted <sup>(1)</sup>		11,009		12,60
Pro forma net loss per share attributable to common shareholders of Biohaven			-	
Pharmaceutical Holding Company Ltd.—basic and diluted (unaudited) <sup>(1)</sup>			\$	(4.4
			-	(
Pro forma weighted average common shares outstanding—basic and diluted (unaudited) <sup>(1)</sup>				14.01
(unaumeu)			_	14,21

(1) See Note 15 to our consolidated financial statements appearing at the end of this prospectus for further details on the calculation of basic and diluted net loss per share attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd. and on the calculation of pro forma basic and diluted net loss per share attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd.

		As of December 31, 2016				
	Actual		Pro Forma <sup>(2)</sup> (in thousands)		Pro Forma As Adjusted <sup>(3)</sup>	
Consolidated Balance Sheet Data:						
Cash	\$	23,565	\$	62,200	\$	209,494
Working capital <sup>(1)</sup>		16,093		54,728		206,372
Total assets		27,017		65,652		212,812
Notes payable, net of discount		4,216		4,216		
Notes payable to related parties		595		595		
Warrant liability		780		780		780
Contingent equity liability		18,938		_		
Convertible preferred shares		43,270		_		
Total shareholders' equity (deficit)		(45,033)		55,810		207,915

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

(2) The pro forma balance sheet data give effect to:

- our sale of 4,305,182 Series A preferred shares in February 2017 for net cash proceeds of \$38.6 million;
- our issuance of an aggregate of 105,009 Series A preferred shares in February 2017 to the placement agents for our Series A financing transaction;
- our issuance of an aggregate of 1,883,523 common shares to BMS and AstraZeneca in connection with this offering pursuant to our license agreements with BMS and AstraZeneca and the reclassification of the contingent equity liability related to such shares; and
- the conversion of all outstanding preferred shares into an aggregate of 9,358,560 common shares upon the closing of this offering.
- (3) The pro forma as adjusted balance sheet data give further effect to (i) our issuance and sale of 9,900,000 common shares in this offering at the initial public offering price of \$17.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, and (ii) the repayment of \$5.6 million of aggregate indebtedness under our credit agreement and our notes payable to related parties using a portion of the net proceeds from this offering.

#### **RISK FACTORS**

Investing in our common shares involves a high degree of risk. You should carefully consider the following risks and all other information contained in this prospectus, including our financial statements and the related notes, before making an investment decision regarding our securities. The risks and uncertainties described below are those significant risk factors, currently known and specific to us, which we believe are relevant to an investment in our securities. If any of these risks materialize, our business, financial condition or results of operations could suffer, the price of our common shares could decline and you could lose part or all of your investment.

#### **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 successfully complete later-stage clinical trials, obtain marketing approvals, 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 \$10.1 million and \$63.5 million for the years ended December 31, 2015 and 2016, respectively. As of December 31, 2016, we had an accumulated deficit of \$75.5 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:

- continue the development of our product candidates, including the initiation of two Phase 3 clinical trials and a long-term safety study of rimegepant for the acute treatment of migraine, the completion of our ongoing Phase 2/3 clinical trial of trigriluzole for the treatment of spinocerebellar ataxia, or SCA, and the initiation and conduct of additional clinical trials and preclinical studies for our other product candidates for various neurological indications;
- make required milestone and royalty payments under the license agreements by which we acquired some of the rights to our product candidates;
- 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;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any product candidate for which we may obtain marketing approval;
- hire additional clinical, regulatory, scientific and accounting personnel; and
- incur additional legal, accounting and other expenses in operating as a public company.

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.

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 U.S. Food and Drug Administration, or FDA, or other regulatory authorities such as the European Medicines Agency, or EMA, 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.

# Even if this offering is successful, 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, in our trigriluzole clinical program, we recently enrolled the first patient in our Phase 2/3 clinical trial of trigriluzole for the treatment of SCA, and, given the small number of SCA patients, we believe that, if successful, this Phase 2/3 clinical trial will be the only pivotal trial necessary to support regulatory approval. Likewise, due to the small number of patients with Rett syndrome, we believe that BHV-5000 will require only a single pivotal trial. 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



trigriluzole or BHV-5000, 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. Furthermore, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company.

As of December 31, 2016, we had cash of \$23.6 million, and in February 2017, we received net cash proceeds of \$38.6 million from the sale of Series A preferred shares in connection with the second and final closing of our Series A preferred share financing. We expect that our existing cash, together with the net proceeds from this offering, will enable us to repay our indebtedness and to fund our operating expenses and capital expenditure requirements through October 31, 2018. 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;
- 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.

Even if this offering is successful, 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, once we are a listed company in the United States, we may not be able to access the capital markets as frequently as comparable U.S. companies. See "—Our status as a British Virgin Islands, or BVI, business company means that our shareholders enjoy certain rights that may limit our flexibility to raise capital, issue dividends and otherwise manage ongoing capital needs" for additional information related to our ability to timely raise capital. 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.

### Our independent registered public accounting firm has included an explanatory paragraph relating to our ability to continue as a going concern in its report on our audited financial statements included in this prospectus.

Our report from our independent registered public accounting firm for the year ended December 31, 2016 includes an explanatory paragraph stating that our recurring losses from operations since inception and required additional funding to finance our operations raise substantial doubt about our ability to continue as a going concern. If we are unable to obtain sufficient funding, our business, prospects, financial condition and results of operations will be materially and adversely affected and we may be unable to continue as a going concern, we may have to liquidate our assets and may receive less than the value at which those assets are carried on our audited financial statements, and it is likely that investors will lose all or a part of their investment. After this offering, future reports from our independent registered public accounting firm may also contain statements expressing substantial doubt about our ability to continue as a going concern. If we seek additional financing to fund our business activities in the future and there remains substantial doubt about our ability to continue as a going concern, investors or other financing sources may be unwilling to provide additional funding to us on commercially reasonable terms or at all.

### 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.

In July 2016, we acquired the rights to rimegepant and another product candidate, BHV-3500, pursuant to a license agreement with Bristol-Myers Squibb Company, or BMS, and in October 2016, we acquired the rights to BHV-5000 pursuant to a license agreement with AstraZeneca AB, or 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. We may also be obligated to pay AstraZeneca up to \$30.0 million in development milestones for 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 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, such license agreements provide BMS and AstraZeneca with rights of first negotiation, triggered by their receipt of a summary of certain top-line data from certain of our clinical trials, to regain

the respective rights we have in-licensed from them. If either BMS or AstraZeneca exercises their right of first negotiation, we will be required to negotiate in good faith with BMS or AstraZeneca, as the case may be, for a specified period of time before we can enter into negotiations with third parties to sublicense these rights. BMS's and 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. Our license agreement with AstraZeneca further provides 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.

Moreover, under our agreement with BMS, 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 competitive compounds related to the CGRP-based mechanism of action of the licensed products. 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 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. These prohibitions could adversely impact or delay our ability to effect certain transactions, such as our ability to acquire or be acquired by a third party.

### 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 your rights as a holder 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 or licensing 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 and none of which have completed a pivotal trial. 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 commencement of two Phase 3 trials of rimegepant, the conducting of our ongoing Phase 2/3 trial of trigriluzole, and other preclinical and clinical activities related to BHV-0223, BHV-5000 and 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 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 each of our product candidates and have not completed Phase 3 clinical trials for any 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. For example, the favorable results of the Phase 2b trial of rimegepant may not be predictive of similar results in subsequent trials. In particular, we are developing a new dosage form of rimegepant for use in our planned Phase 3 clinical trials of rimegepant. We cannot be certain that we will observe the same results in our Phase 3 trials with the new dosage form as we did in the Phase 2b clinical trials of rimegepant. In later-stage clinical trials, we will likely be subject to more rigorous statistical analyses than in completed earlier 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.

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 other clinical trial protocols, and the rate of dropout among clinical trial participants. 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 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.

### 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 delay or refusal of regulators or institutional review boards, or 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 organizations, or 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, or 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.

We will need to take a variety of steps before commencing our two planned Phase 3 clinical trials and 12-month safety study of rimegepant and our planned clinical trials of BHV-0223 and BHV-5000. With

respect to rimegepant, we had an end of Phase 2 meeting with the FDA in March 2017 at which we reviewed the Phase 2b clinical trial data with the FDA and presented our overall plan for our planned Phase 3 clinical trials and safety study and our proposed path to registration. At the meeting, we agreed to submit our trial protocols to the FDA prior to the commencement of our Phase 3 trials. The FDA could disagree with the proposed design of our planned Phase 3 clinical trials and safety study and could require, in any trial or all trials, a larger number of patients or a longer course of treatment than our current expectations. If the FDA takes such positions, the costs of our planned Phase 3 clinical trials and safety study and the potential commercialization of rimegepant could be delayed. The FDA also may require that we conduct additional clinical, nonclinical or manufacturing validation studies and submit such data before it will consider a NDA.

In addition, prior to commencing our two planned Phase 3 clinical trials, we will have to:

- obtain sufficient clinical supply of rimegepant; and
- complete a study to compare the pharmacokinetics for a new formulation of rimegepant with the prior formulation. We cannot be certain that the results observed in our Phase 2b clinical trial will be replicated with the new formulation.

In order to commence our planned clinical trials of BHV-0223 and BHV-5000, we will have to complete development of a commercial-grade formulation and obtain sufficient clinical supply of both product candidates.

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.

#### 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 a New Drug Application, or NDA, from the FDA or approval from the EMA 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 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 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 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 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 or the applicable foreign regulatory agency that our product candidates are safe and effective for their proposed indications;
- the FDA's, EMA'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 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 or the applicable foreign regulatory agency's requirement for additional preclinical studies or clinical trials;
- the FDA's, EMA'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 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 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 ongoing Phase 2/3 clinical trial for trigriluzole for the treatment of SCA, the FDA has stated that elements of the SARA (i.e., gait, stance, sitting and speech disturbance) appear capable of reflecting a clinically meaningful benefit for patients depending on how the scoring of these items is defined. If the scoring categories are based on clinically important distinctions, use of these items as a primary endpoint in studies intended to support approval could be appropriate. However, the FDA has stated its concern that our use of the SARA scale, as currently constructed, as a primary endpoint is not appropriate in this trial. No drug has been approved for the treatment of SCA and, therefore, a clear regulatory pathway for approval has not previously been established. Although we selected the SARA scale, which is a validated scale that has been used in a third-party clinical trial for the treatment of hereditary ataxias (including SCA), as the primary outcome measure for the trial based on advice of an advisory panel of ataxia experts, we plan to continue to interact with the FDA to discuss its concerns and consider incorporating any feedback in our analysis of the clinical trial data that we collect and measure

with the SARA. Because we have already begun our Phase 2/3 clinical trial and the FDA has not suggested an alternative scale that it believes would be acceptable to assess clinical benefit in SCA, we have limited options to incorporate an alternate scale that has been validated and is accepted by the field's experts as measuring clinically meaningful changes. As such, we cannot guarantee that the FDA or any future advisory committee will be satisfied with our approach using the SARA. We cannot guarantee that any regulatory agency or future advisory committee would interpret a successful outcome using the SARA as our primary measure in the same fashion that we would.

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 treatment of acute 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 including, at a minimum, 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, or 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 moderate to severe migraine headache. 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 study. The placebo effect also tends to have a more significant impact on clinical trials involving subjective measures such as pain.

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. 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. Even though no patient treated with rimegepant in the Phase 2b trial had liver enzyme elevation that exceeded the level that is considered by the FDA to be a potentially meaningful indicator of severe drug-induced liver injury, we cannot guarantee that these safety and tolerability results will be replicated in our Phase 3 trials, 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 neardaily 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.

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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. Serious 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 study 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;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- 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. 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 investigatorsponsored 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.

#### **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 CoLucid Pharmaceuticals, as well as other small molecule CGRP receptor antagonists such as ubrogepant, being developed by Allergan. These 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, we expect that our migraine

product candidates will also compete with opioids and other analgesics, monoclonal antibodies in development and Botox and other treatments that have been approved by the FDA for migraine.

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, which is currently the only approved drug for the treatment of ALS in the United States. We are aware of at least two other companies marketing or planning to market new formulations of riluzole. MonoSol Rx has filed an IND with the FDA to conduct clinical trials for a riluzole oral soluble film, and 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. To our knowledge, no other companies are marketing sublingual formulations 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 has obtained orphan designation for Teglutik, and is eligible to obtain orphan exclusivity subject to a showing of clinical superiority to riluzole. If Teglutik is shown to be clinically superior to Rilutek and receives marketing approval before BHV-0223, then BHV-0223 may need to demonstrate clinical superiority to Teglutik to receive marketing approval.

With respect to trigriluzole, which we are currently developing for the treatment of ataxias, with SCA as our initial indication, there are currently no approved drug treatments for spinocerebellar ataxias in the United States. 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.

If we expand our development of trigriluzole, 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.

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 discovery and development of novel compounds or to inlicense 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 are 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 governmental authorities, private health insurers and other organizations will have an effect on our ability to successfully commercialize, 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 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 and other therapies as substitutable 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. 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 payors, such as the Medicare and Medicaid 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 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, or 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 request 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.

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 no 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 no 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 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 an 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 trigriluzole, 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 or 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 FCCDC, pursuant to which we were assigned intellectual property rights relating to trigriluzole, 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 a license agreement with AstraZeneca, pursuant to which we were granted an exclusive license to use their Zydis technology in the development of BHV-5000. 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. See "Business—License Agreements" for a more detailed description of our current license agreements.

#### 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 intend to conduct our future clinical trials, including our two planned Phase 3 clinical trials of rimegepant and our Phase 2/3 clinical trial of trigriluzole, using our own clinical resources while also leveraging expertise and assistance from 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 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 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. 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 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;

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- 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 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 not be able 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 Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the 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 agree to offer 50% 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 a Center for Medicare Innovation at the Centers for Medicare & 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. In addition, the current administration and Congress will likely continue to seek legislative and regulatory changes, including repeal and replacement of certain provisions of the ACA. In January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In March 2017, following the passage of the budget resolution for fiscal year 2017, the U.S. House of Representatives introduced legislation known as the American Health Care Act, which, if enacted, would have amended or repealed significant portions of the ACA. However, consensus over the scope and content of the American Health Care Act could not be reached by its proponents in the U.S. House of Representatives. Thus, the proposed legislation has been withdrawn and the prospects for legislative action on this bill are uncertain. Congress could consider other legislation to repeal or replace certain elements of the ACA. We continue to evaluate the effect that the ACA and its possible repeal and replacement has on our business.

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, will remain in effect through 2025 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 may develop new payment and delivery models, such as bundled payment models. The U.S. Department of Health and Human Services, or HHS, set a goal of moving 30% of Medicare payments to alternative payment models tied to the quality or value of services by 2016 and 50% of Medicare payments into these alternative payment models by the end of 2018. In March, HHS announced that it has achieved its goal for 2016. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. 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.

Individual states in the United States have also become 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. 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.

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 everincreasing 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,

and proposed sales, marketing and education programs and constrain the business of 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 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, or 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, or 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 the Final HIPAA Omnibus Rule, i.e. health plans, healthcare clearinghouses and 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 legislation commonly referred to as Physician Payments Sunshine Act, enacted as part of the ACA, and its implementing regulations, which requires 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 the 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; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and
- European and other foreign law equivalents of each of the laws, including reporting requirements detailing interactions with and payments to healthcare providers.

Ensuring that our internal operations 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 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 trigriluzole in SCA and BHV-0223 in ALS. 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 orphan drug exclusivity for BHV-0223 for ALS is contingent upon a showing that BHV-0223 is clinically superior to Rilutek 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 riluzole, we will not be entitled to the benefits of 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.

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.

#### **Risks Related to Our Intellectual Property**

### If we are unable to obtain and maintain patent protection for our technology and product candidates, or if the scope of the patent protection obtained is not sufficiently broad, we may not be able to compete effectively in our markets.

We rely upon a combination of patents, trade secret protection and confidentiality agreements 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 position by filing and in-licensing patent applications in the United States and abroad related to our development programs and product candidates.

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. Prosecution of much of our patent portfolio is at a very early stage. None of our owned or in-licensed patents claiming BHV-5000, trigriluzole or BHV-0223 have issued, and applications under the Patent Cooperation Treaty, or PCT, remain pending with respect to trigriluzole and BHV-0223. As applicable deadlines under the PCT become due, we will have to decide whether and where to pursue patent protection for the various inventions claimed in our patent portfolio, and we will only have the opportunity to obtain patents in those jurisdictions where we pursue protection.

It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late 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 in the United States or in other foreign countries. Our patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, a patent issues from such applications, and then only to the extent the issued claims cover the technology.

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 and has in recent years been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, EU patent law restricts the patentability of methods of treatment of the human body more than U.S. law does. 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 do successfully issue 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 commercialize our technology or products and 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 trigriluzole and BHV-0223 only protect or seek to protect the formulation 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 PCT applications. These families of patent applications cover trigriluzole 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. For example, U.S. applications filed before November 29, 2000 and certain U.S. applications filed after that date that will not be filed outside the United States remain confidential until patents issue. 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 licensor 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. See "Business—License Agreements" for a detailed description of our rights and obligations under these license agreements. 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 natural 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. 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 thus attacked, 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, provide a barrier to entry against our competitor or potential competitors 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 patent laws or patent jurisprudence could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical

industry involve both technological complexity and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time-consuming and inherently uncertain. In addition, the America Invents Act, or the AIA, was signed into law on September 16, 2011, and many of the substantive changes became effective on March 16, 2013.

An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to 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. A third party that files a patent application in the U.S. Patent and Trademark Office, or USPTO, after that date but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application, but circumstances could prevent us from promptly filing patent applications on our inventions.

Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and providing additional opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, 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. The AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

The USPTO has developed in the last few years regulations and procedures to govern administration of the AIA, and many of the substantive changes to patent law associated with the AIA, and, in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the AIA will have on the operation of our business. However, the AIA and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors' or collaboration partners' patent applications and the enforcement or defense of our or our licensors' or collaboration partners' issued patents, all of which could have an adverse effect on our business and financial condition.

Additionally, the U.S. Supreme Court has ruled on several patent cases in recent years, such as 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. Similarly, the complexity and uncertainty of European patent laws has also increased in recent years. For example, the April 2010 amendment of the European Patent Convention, which limited the time permitted for filing divisional applications, was subsequently abrogated. This amendment and subsequent abrogation illustrates the uncertainty involved in the prosecution of European patent laws. In addition, the European patent system is relatively stringent in the type of amendments that are allowed during prosecution. These changes could limit our ability to obtain new patents in the future that may be important for our business.

# 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, LLC, 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, or 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.

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, oppositions 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. 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 competitive technologies that fall outside of 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 noncompliance 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. Each of these officers may currently terminate their employment with us at any time and will continue to be able to do so after the closing of this offering. 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, or 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, 2016, we had 12 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 that will become effective at the completion of this offering, 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 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 may 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.

#### **Risks Related to This Offering and Our Common Shares**

### There has been no public market for our common shares prior to this offering, and an active market in the shares may not develop or be liquid enough for investors to resell our common shares quickly or at the market price.

Prior to this offering, there has been no public market for our common shares. We cannot predict the extent to which an active market for our common shares will develop or be sustained after this offering, or how the development of such a market might affect the market price for our common shares. The initial public offering price of our common shares in this offering was agreed upon between us and the underwriters based on a number of factors, including market conditions in effect at the time of the offering, which may not be indicative of the price at which our shares will trade following completion of the offering. If an active market for our common shares does not develop or is not sustained, it may be difficult for you to sell shares you purchased in this offering at an attractive price or at all.

Certain of our existing principal shareholders, directors and their affiliated entities have agreed to purchase an aggregate of 3,142,117 common shares in this offering at the initial public offering price per share. Such purchases will reduce the available public float for our shares because these entities will be restricted from selling the shares by a lock-up agreement they have entered into with the underwriters and/or by restrictions under applicable securities laws. As a result, the purchases of shares by such entities in this offering will reduce the liquidity of our common shares compared to what it would have been had these shares been purchased by investors that were not affiliated with us.

#### The price of our common shares is likely to be volatile and may fluctuate due to factors beyond our control.

The share price of publicly traded emerging biopharmaceutical and drug discovery and development companies has been highly volatile and is likely to remain highly volatile in the future. The market price of our common shares may fluctuate significantly due to a variety of factors, including:

- positive or negative 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;
- failure to meet or exceed expectations of the investment community;
- 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;
- 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. In addition, the stock market in general, and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies.

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 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. We do not currently have and may never obtain research coverage by equity research analysts. If no or too few securities or industry analysts commence coverage of us, the trading price for our common shares would likely be negatively affected. In the event securities or industry analysts initiate coverage, if one or more of the analysts who cover us downgrade our common shares or publish inaccurate or unfavorable research about our business, the price of our common shares would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, demand for our common shares could decrease, which might cause the price of our common shares and trading volume to decline.

### We will 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, we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the stock exchange on which our common shares are listed, and other applicable securities rules and regulations impose various requirements on public companies, including the establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management, board of directors and other personnel will need to devote a substantial amount of time to these compliance initiatives. 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 and more expensive for us to obtain director and of directors. However, 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.

### Concentration of ownership of our common shares among our existing executive officers, directors and principal shareholders may prevent new investors from influencing significant corporate decisions.

Following this offering, our directors and executive officers, and entities affiliated with them, as well as holders of more than 5% of our outstanding common shares, in the aggregate will beneficially own 51.3% of our common shares, after giving effect to the issuance of shares in this offering but without giving effect to any purchases by such persons or entities in the offering or the directed share program. These shareholders, acting together, will 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. Certain of these persons and entities have indicated an interest in purchasing additional common shares in this offering, which would increase their ownership percentage, and they may further increase their ownership in our company pursuant to the directed share program.

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 price at which shares are being sold in this offering 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.

## Anti-takeover 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 association that will become effective upon the closing of this offering 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.

#### Future sales of our common shares in the public market could cause our share price to fall.

Sales of a substantial number of our common shares in the public market after this offering, 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. Upon the closing of this offering, we will have 34,230,583 common shares outstanding, assuming no exercise of outstanding options or the underwriters' option to purchase additional shares.

All of the common shares sold in this offering will be freely tradable without restrictions or further registration under the Securities Act except for any shares held by our affiliates as defined in Rule 144 under the Securities Act. A total of 24,330,583, or approximately 71.1%, of the common shares outstanding immediately after this offering will be restricted as a result of securities laws, lock-up agreements or other contractual restrictions that restrict transfers for 180 days after the date of this prospectus.

The underwriters may, in their sole discretion, release all or some portion of the shares subject to lock-up agreements with the underwriters prior to expiration of the lock-up period. See "Shares Eligible for Future Sale."

The holders of approximately 23,000,000, or approximately 67.2%, of the common shares outstanding immediately after this offering will be entitled to rights with respect to registration of such shares under the Securities Act pursuant to an investors' rights agreement between such holders and us. See "Description of Share Capital—Registration Rights." If such holders, by exercising their registration rights, sell a large number of shares, the market price for our common shares could be harmed. If we file a registration statement for the purpose of selling additional shares to raise capital and are required to include shares held by these holders pursuant to the exercise of their registration rights, our ability to raise capital may be impaired. We will also file a registration statement on Form S-8 under the Securities Act to register shares for issuance under our equity incentive plans, including our 2014 Equity Incentive Plan and our 2017 Equity Incentive Plan will provide for automatic increases in the shares reserved for issuance under the plan which could result in additional dilution to our shareholders. Once we register these shares, they can be freely sold in the public market upon issuance and vesting, subject to any lock-up restrictions of the holder.

### 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.

#### If you purchase common shares in this offering, you will suffer immediate dilution of your investment.

The initial public offering price of our common shares is substantially higher than the pro forma as adjusted net tangible book value per share. Therefore, if you purchase common shares in this offering, you will pay a price per share that substantially exceeds the book value per share of our tangible assets, after subtracting our liabilities, after this offering. Based on the initial public offering price of \$17.00 per share, you will experience immediate dilution of \$10.93 per common share, representing the difference between our pro forma as adjusted net tangible book value per share after giving effect to this offering and the initial public offering price. In addition, purchasers of common shares in this offering will have contributed approximately 62.8% of the aggregate price paid by all purchasers of our common shares but will own only approximately 28.9% of our common shares outstanding after this offering. To the extent options or warrants are exercised, you will incur further dilution. See the section of this prospectus entitled "Dilution."

#### We will have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common shares. We intend to use the net proceeds from this offering to conduct our two planned Phase 3 clinical trials of rimegepant for the acute treatment of migraine; to fund continued research and development of BHV-3500 for the prevention of chronic and episodic migraine; to complete our ongoing Phase 2/3 clinical trial of trigriluzole for the treatment of spinocerebellar ataxia; to fund continued research and development of BHV-5000 for the treatment of symptoms associated with Rett syndrome, including completion of our planned Phase 1 clinical trial for this indication; to fund other research and development activities, including development of BHV-0223 for the treatment of ALS; to repay indebtedness outstanding under our credit agreement and notes payable to related parties; and for working capital and other general corporate purposes, including the satisfaction of any milestone payment obligations under our license agreements. The failure by our management to apply these funds effectively could result in financial losses that could have an adverse effect on our business, cause the price of our common shares to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

### We are an "emerging growth company," and we cannot be certain if the reduced reporting requirements applicable to "emerging growth companies" will make our common shares less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For as long as we continue to be an "emerging growth company," we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not "emerging growth companies," including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. As an "emerging growth company," we are required to report only two years of financial results and selected financial data compared to three and five years, respectively, for comparable data reported by other public companies. We may take advantage of these exemptions until we are no longer an "emerging growth company." We could be an "emerging growth company" for up to five years, although circumstances could cause us to lose that status earlier, including if the aggregate market value of our common shares held by non-affiliates exceeds \$700 million as of any June 30 (the end of our second fiscal quarter) before that time, in which case we would no longer be an "emerging growth company" as of the following December 31 (our fiscal year end). We cannot predict if investors will find our common shares less attractive because we may rely on these exemptions. If

some investors find our common shares less attractive as a result, there may be a less active trading market for our common shares and the price of our common shares may be more volatile.

We have identified material weaknesses in our internal control over financial reporting. If we are unable to remediate these material weaknesses, or if we experience additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect investor confidence in us and, as a result, the value of our common shares.

We have identified material weaknesses in our internal control over financial reporting. A material weakness is a deficiency, or 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.

If we are unable to remediate these material weaknesses, or if we experience additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect investor confidence in us and, as a result, the value of our common shares.

Prior to the completion of this offering, we have been a private company with limited accounting personnel and other resources to address our internal control over financial reporting. In preparation of our financial statements to meet the requirements of this offering, we determined that material weaknesses in our internal control over financial reporting existed during each of fiscal 2014 and 2015 and remained unremediated as of December 31, 2016. These material weaknesses in our internal control over financial reporting are described below.

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 weaknesses:

- 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.

These material weaknesses contributed to several accounting adjustments being made to our financial statements for the years ended December 31, 2014, 2015 and 2016 and the nine months ended September 30, 2015 and 2016 related to our accounting for our license agreement obligations, income taxes, variable interest entities, share-based compensation, derivative liabilities, warrants and contingent equity, research and development expense, general and administrative expense, and other income (expense). In addition, these material weaknesses contributed to the restatement of our financial statements for the nine months ended September 30, 2016 related to our accounting for license agreement obligations.

We identified an additional material weakness as a result of the material weakness in our control environment in that 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.

These IT deficiencies did not result in a material misstatement to our financial statements; however, the deficiencies, when aggregated, could impact the effectiveness of IT-dependent controls, such as automated controls that address the risk of material misstatement to one or more assertions, along with the IT controls and underlying data that support the effectiveness of system-generated data and reports.

Each of the control deficiencies could result in a misstatement of these accounts or disclosures that would result in a material misstatement of our annual or interim consolidated financial statements that would not be prevented or detected, and accordingly, we determined that these control deficiencies constitute material weaknesses.

We have initiated remediation efforts focused on improving our internal control over financial reporting and to specifically address the control deficiencies that led to our material weaknesses. These efforts include the following:

- Initial investment in finance and accounting organization, including:
  - Hiring of our chief financial officer in May 2016; and
  - Hiring of a corporate controller in January 2017.
- Retaining a technical accounting consulting firm in October 2016 to provide additional depth and breadth in our technical accounting and financial reporting capabilities. We intend to continue this arrangement until permanent technical accounting resources are identified and hired.
- Initiating design and implementation of our financial control environment, including policies and procedures, controls, reporting and analysis, and segregation of duties.

We cannot assure you that the measures we have taken to date, and actions we may take in the future, will be sufficient to remediate the control deficiencies that led to our material weaknesses in our internal control over financial reporting or that they will prevent or avoid potential future material weaknesses. In addition, neither our management nor an independent registered public accounting firm has ever performed an evaluation of our internal control over financial reporting in accordance with the provisions of the Sarbanes-Oxley Act because no such evaluation has been required. Had we or our independent registered public accounting firm performed an evaluation of our internal control over financial reporting in accordance with the provisions of the Sarbanes-Oxley Act, additional material weaknesses may have been identified. If we are unable to successfully remediate our existing or any future material weaknesses in our internal control over financial reporting, or identify any additional material weaknesses, the accuracy and timing of our financial reporting may be adversely affected, we may be unable to maintain compliance with securities law requirements regarding timely filing of periodic reports in addition to applicable stock exchange listing requirements, investors may lose confidence in our financial reporting, and our share price may decline as a result.

# You may have fewer protections as a shareholder of our company, as the rights of shareholders under British Virgin Islands law differ from those under U.S. law.

Our corporate affairs will be governed by our memorandum and articles of association, the BVI Business Companies Act, 2004, or 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. For a discussion of significant differences between the provisions of the BVI Act and the laws applicable to companies incorporated in the United States and their shareholders, see "Description of Share Capital—Differences in Corporate Law."

# 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 British Virgin Island 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 favour 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.

# It may be difficult to enforce a U.S. or foreign judgment against us, our directors and officers named in this prospectus 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 the United States, and a "foreign corporation" if it is incorporated or organized in a non-U.S. jurisdiction. Because we are a British Virgin Islands incorporated entity, we would be classified as a foreign corporation under these general rules. Section 7874 of the Code, or 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'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. 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, the Company entered into an agreement with the stockholders of Biohaven Pharmaceuticals, Inc., a Delaware corporation, or 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 Company promissory notes

to each BPI stockholder (see "Certain Relationships and Related Party Transactions—Transactions with Biohaven Pharmaceuticals, Inc."). Although the Company 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.

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, following this offering, 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, or 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, 2016, and do not currently expect to be a PFIC for our current taxable year 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 this offering.

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", or 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.

For further discussion of the PFIC rules and the adverse U.S. federal income tax consequences in the event we are classified as a PFIC, see the section of this prospectus entitled "Material United States Federal Income Considerations For U.S. Holders—Passive Foreign Investment Company Considerations."

# INFORMATION REGARDING FORWARD-LOOKING STATEMENTS

This prospectus includes forward-looking statements. All statements other than statements of historical facts contained in this prospectus, including statements regarding our future results of operations and financial position, strategy and plans, and our expectations for future operations, are forward-looking statements. The words "believe," "may," "will," "estimate," "continue," "anticipate," "design," "intend," "expect," "could," "plan," "potential," "predict," "seek," "should," "would" or the negative version of these words and similar expressions are intended to identify forward-looking statements. We have based these forward-looking statements on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, strategy, short- and long-term business operations and objectives, and financial needs. These forward-looking statements include, but are not limited to, statements concerning the following:

- our plans to develop and commercialize our product candidates;
- our planned clinical trials for our rimegepant, trigriluzole, BHV-0223 and BHV-5000 development programs;
- the timing of the availability of data from our clinical trials;
- the timing of our planned regulatory filings;
- 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.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including those described in "Risk Factors." Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this prospectus may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. Moreover, except as required by law, neither we nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this prospectus to conform these statements to actual results or to changes in our expectations.

You should read this prospectus and the documents that we reference in this prospectus and have filed with the SEC as exhibits to the registration statement of which this prospectus is a part with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect.

## **INDUSTRY AND MARKET DATA**

We obtained the industry, market and competitive position data used throughout this registration statement from our own internal estimates and research, as well as from industry and general publications, in addition to research, surveys and studies conducted by third parties. Internal estimates are derived from publicly available information released by industry analysts and third-party sources, our internal research and our industry experience, and are based on assumptions made by us based on such data and our knowledge of our industry and market, which we believe to be reasonable. In addition, while we believe the industry, market and competitive position data included in this registration statement is reliable and is based on reasonable assumptions, such data involves risks and uncertainties and is subject to change based on various factors, including those discussed in "Risk Factors." These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

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# **USE OF PROCEEDS**

We estimate that the net proceeds from our issuance and sale of common shares in this offering will be approximately \$152.9 million, or approximately \$176.4 million if the underwriters exercise their over-allotment option in full, based upon the initial public offering price of \$17.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We currently estimate that we will use the net proceeds from this offering, together with our existing cash, as follows:

- approximately \$73.1 million to fund continued research and development of rimegepant, including initiating and completing our two planned Phase 3 clinical trials for the acute treatment of migraine, and initiating our planned long-term safety study of rimegepant;
- approximately \$24.2 million to fund continued research and development of BHV-3500 for the prevention of chronic and episodic migraine;
- approximately \$9.6 million to complete our ongoing Phase 2/3 clinical trial of trigriluzole for the treatment of SCA;
- approximately \$10.3 million to fund continued research and development of BHV-5000 for the treatment of breathing irregularities associated with Rett syndrome, including completion of our planned Phase 1 clinical trial for this indication;
- approximately \$5.6 million to repay aggregate indebtedness under our credit agreement with Wells Fargo Bank, National Association, or Wells Fargo, and our notes payable to related parties;
- approximately \$4.1 million to satisfy our remaining obligation to purchase shares of capital stock of Kleo Pharmaceuticals, Inc., a privately held preclinical-stage company; and
- the remainder to fund other research and development activities, including the development of BHV-0223 for the treatment of ALS, as well as for working capital and other general corporate purposes, including the satisfaction of any milestone payment obligations under our license agreements.

In the ordinary course of our business, we expect to from time to time evaluate the acquisition of, investment in or in-license of complementary products, technologies or businesses, and we could use a portion of the net proceeds from this offering for such activities. We currently do not have any agreements, arrangements or commitments with respect to any potential acquisition, investment or license, other than the Kleo investment described above.

This expected use of net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. Predicting the cost necessary to develop product candidates can be difficult and the amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development, the status of and results from clinical trials, any collaborations that we may enter into with third parties for our product candidates and any unforeseen cash needs.

Based on our current operational plans and assumptions, we expect that the net proceeds from this offering, together with our existing cash, will be sufficient to fund our operations through October 31, 2018, including the repayment of our outstanding debt, and, with respect to our planned and ongoing clinical trials, will be sufficient to enable us to complete our two planned Phase 3 clinical trials of rimegepant and complete our Phase 2/3 clinical trial of trigriluzole. However, we expect that we will require additional funds to complete the development of rimegepant for the acute treatment of migraine, including for the completion of our planned long-term safety study. With respect to the continued research and development of BHV-3500 and BHV-5000, we expect that we may require additional funds as these programs progress, the amounts of which will depend on the ultimate clinical development paths we

pursue. However, our plans and assumptions could be wrong and we may need to raise additional capital in order to complete our planned and ongoing trials and any potential future trials that may be required by regulatory authorities. We may need to raise additional capital through public and private equity offerings, debt financings, strategic partnerships, alliances and licensing arrangements, or a combination of the above.

We incurred the indebtedness under the one-year credit agreement with Wells Fargo in August 2016 in the principal amount of \$5.0 million to satisfy our payment obligations under our license agreement with BMS. The one-year credit agreement matures on August 30, 2017, and borrowings under the agreement bear interest at a rate equal to monthly LIBOR plus 1.50% per annum. As of December 31, 2016, the interest rate applicable to the borrowings under the one-year credit agreement was 2.27% per annum. In connection with this credit agreement, Wells Fargo required that we obtain a personal guaranty of our loan obligations from one of our directors, John Childs. Another one of our directors, Gregory Bailey, provided a further guaranty related to the credit agreement. We incurred the indebtedness under our notes payable in the aggregate amount of \$0.6 million in consideration for the acquisition of 100% of the capital stock of BPI on December 31, 2016. We issued the notes to the holders of the capital stock of BPI, which consisted of Declan Doogan, the chairman of our board of directors; family trusts associated with Vlad Coric, our chief executive officer and one of our directors; and a family trust associated with Robert Berman, our chief medical officer. The notes mature on December 31, 2021, but are mandatorily payable upon the consummation of this offering, and the interest on the notes accrues at a rate of 4.5% per annum.

As of December 31, 2016, we owned approximately 18.6% of the outstanding shares of Kleo and two of our outside directors serve as Kleo directors, resulting from our arm's-length investment in Kleo in August 2016. In connection with our initial investment, we committed to make additional investments totaling \$5.5 million in Kleo, subject to certain conditions, and in March 2017, we satisfied our first purchase obligation by purchasing 1,375,000 shares of Kleo common stock for cash consideration of \$1.4 million.

Our management will have broad discretion in the application of the net proceeds from this offering, and investors will be relying on the judgment of our management regarding the application of the net proceeds from this offering. The timing and amount of our actual expenditures will be based on many factors, including cash flows from operations and the anticipated growth of our business. Pending these uses, we plan to hold these 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.

# **DIVIDEND POLICY**

We have never declared or paid any dividends on our common shares. We anticipate that we will retain all of our future earnings, if any, for use in the operation and expansion of our business and do not anticipate paying cash dividends in the foreseeable future.

# CAPITALIZATION

The following table sets forth our cash and our capitalization as of December 31, 2016:

- on an actual basis;
- on a pro forma basis to give effect to:
  - our sale of 4,305,182 Series A preferred shares in February 2017 for net cash proceeds of \$38.6 million;
  - our issuance of an aggregate of 105,009 Series A preferred shares in February 2017 to the placement agents for our Series A financing transaction;
  - our issuance of an aggregate of 1,883,523 common shares to BMS and AstraZeneca in connection with this offering pursuant to our license agreements with BMS and AstraZeneca and the reclassification of the contingent equity liability related to such shares;
  - the conversion of all outstanding preferred shares into an aggregate of 9,358,560 common shares upon the closing of this offering; and
  - the filing and effectiveness of our amended and restated memorandum and articles of association immediately prior to the closing of this offering; and
- on a pro forma as adjusted basis to give further effect (i) to our issuance and sale of 9,900,000 common shares in this offering at the initial public offering price of \$17.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, and (ii) the repayment of \$5.6 million of aggregate indebtedness under our credit agreement and our notes payable to related parties using a portion of the net proceeds from this offering.

You should read the following table in conjunction with our consolidated financial statements and the related notes appearing at the end of this prospectus, and the sections of this prospectus titled "Selected

Consolidated Financial Data," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Description of Share Capital."

	As of December 31, 2016								
		Actual	_	ro Forma	As	ro Forma Adjusted <sup>(1)</sup>			
	(in thousands, except s share data								
Cash	\$	23,565	\$	62,200	\$	209,494			
Notes payable, net of discount	\$	4,216	\$	4,216	\$				
Notes payable to related parties		595		595					
Warrant liability		780		780		780			
Contingent equity liability		18,938				_			
Series A convertible preferred shares, no par value; 11,242,172									
shares authorized, 4,948,369 shares issued and outstanding,									
actual; no shares authorized, issued or outstanding, pro forma									
and pro forma as adjusted		43,270		—		—			
Shareholders' equity (deficit):									
Preferred shares, no par value; no shares authorized, issued or									
outstanding, actual; 10,000,000 shares authorized and no									
shares issued or outstanding, pro forma and pro forma as									
adjusted						_			
Common shares, no par value; 38,000,000 shares authorized,									
13,088,500 shares issued and outstanding, actual;									
200,000,000 shares authorized, 24,330,583 shares issued and									
outstanding, pro forma; 200,000,000 shares authorized,									
34,230,583 shares issued and outstanding, pro forma as		19,944		120,787		272 676			
adjusted Additional paid-in capital		19,944		120,787		273,676 10,479			
Accumulated deficit		(75,456)				(76,240)			
	_	<u> </u>	_	(75,456)					
Total shareholders' equity (deficit)	¢	(45,033)	¢	55,810	¢	207,915			
Total capitalization	\$	22,766	\$	61,401	\$	208,695			

(1) Immediately prior to the reclassification of the contingent equity liability in connection with this offering, the contingent equity liability will be remeasured to fair value and the change in fair value will be recorded as other expense in our consolidated statement of operations. The pro forma as adjusted amount of common shares and of accumulated deficit does not reflect the impact of this final change-in-fair-value adjustment. However, as such amounts will equally offset, the final adjustment will have no impact on the pro forma as adjusted amount of total shareholders' equity or of total capitalization.

The number of common shares outstanding in the table above does not include:

- 3,864,425 common shares issuable upon exercise of stock options outstanding as of December 31, 2016, at a weighted average exercise price of \$3.61 per share;
- 600,000 common shares issuable upon exercise of warrants outstanding as of December 31, 2016, at an exercise price of \$5.60 per share;
- 1,034,805 common shares reserved and available as of December 31, 2016 for future issuance under our 2014 Equity Incentive Plan, as amended (of which options to purchase an aggregate of 1,034,433 common shares were issued subsequent to December 31, 2016, at a weighted average exercise price of \$10.14 per share); and
- 2,712,741 common shares reserved for future issuance under our 2017 Equity Incentive Plan, or the 2017 Plan, and 339,139 common shares reserved for future issuance under our 2017 Employee Share Purchase Plan, or ESPP, each of which became effective upon the signing of the underwriting agreement related to this offering, as well as any automatic increases in the number of common shares reserved for future issuance under the 2017 Plan and the ESPP.

# **DILUTION**

If you invest in our common shares in this offering, your ownership interest will be diluted immediately to the extent of the difference between the initial public offering price per common share and the pro forma as adjusted net tangible book value per common share immediately after this offering.

Our historical net tangible book value (deficit) as of December 31, 2016 was \$(45.2) million, or \$(3.45) per common share. Our historical net tangible book value (deficit) is the amount of our total tangible assets less our total liabilities and the carrying value of convertible preferred shares, which is not included within shareholders' equity (deficit). Historical net tangible book value per share represents historical net tangible book value (deficit) divided by the 13,088,500 common shares outstanding as of December 31, 2016.

Our pro forma net tangible book value as of December 31, 2016 was \$55.7 million, or \$2.29 per common share. Pro forma net tangible book value represents the amount of our total tangible assets less our total liabilities, after giving effect to:

- our sale of 4,305,182 Series A preferred shares in February 2017 for net cash proceeds of \$38.6 million;
- our issuance of an aggregate of 105,009 Series A preferred shares in February 2017 to the placement agents for our Series A financing transaction;
- our issuance of an aggregate of 1,883,523 common shares to BMS and AstraZeneca in connection with this offering pursuant to our license agreements with BMS and AstraZeneca and the reclassification of the contingent equity liability related to such shares; and
- the conversion of all outstanding preferred shares into an aggregate of 9,358,560 common shares upon the closing of this offering.

Pro forma net tangible book value per share represents our pro forma net tangible book value divided by the total number of shares outstanding as of December 31, 2016, after giving effect to the pro forma adjustments described above.

After giving further effect to (i) our issuance and sale of 9,900,000 common shares in this offering at the initial public offering price of \$17.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, and (ii) the repayment of \$5.6 million of aggregate indebtedness under our credit agreement and our notes payable to related parties using a portion of the net proceeds from this offering, our pro forma as adjusted net tangible book value as of December 31, 2016 would have been \$207.9 million, or \$6.07 per share. This represents an immediate increase in pro forma as adjusted net tangible book value per share of \$3.78 to existing shareholders and immediate dilution in pro forma as adjusted net tangible book value per share of \$10.93 to new investors purchasing common shares in this offering. Dilution per share to new investors is determined by subtracting pro forma as adjusted net tangible book value per share after this offering from the initial

public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis:

Initial public offering price per share	5	§ 17.00
Historical net tangible book value (deficit) per share as of December 31, 2016	\$ (3.45)	
Increase per share attributable to the pro forma adjustments described above	5.74	
Pro forma net tangible book value per share as of December 31, 2016	2.29	
Increase in pro forma as adjusted net tangible book value per share attributable to		
new investors purchasing common shares in this offering and the repayment of		
our indebtedness	3.78	
Pro forma as adjusted net tangible book value per share after this offering		6.07
Dilution per share to new investors purchasing common shares in this offering	3	\$ 10.93

If the underwriters exercise their over-allotment option in this offering in full, the pro forma as adjusted net tangible book value per share after this offering would be \$6.48 per share, and the dilution in pro forma as adjusted net tangible book value per share to new investors purchasing common shares in this offering would be \$10.52 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

The following table summarizes, on the pro forma as adjusted basis described above, the total number of common shares purchased from us on an as converted to common share basis, the total consideration paid or to be paid, and the average price per share paid or to be paid by existing shareholders and by new investors in this offering at the initial public offering price of \$17.00 per share, before deducting underwriting discounts and commissions and estimated offering expenses payable by us:

	Shares Pur	chased	Total Consid	eration	<b>Average Price</b>		
	Number	Percentage	Amount	Percentage	Per Share		
Existing shareholders	24,330,583	71.1%\$	99,755,146	37.2%\$	4.10		
New investors	9,900,000	28.9	168,300,000	62.8 \$	17.00		
Total	34,230,583	100.0%\$	268,055,146	100.0%			

The table above assumes no exercise of the underwriters' over-allotment option in this offering. If the underwriters' over-allotment option is exercised in full, the number of common shares held by new investors purchasing common shares in this offering would be increased to 31.9% of the total number of common shares outstanding after this offering, and the number of shares held by existing shareholders would be reduced to 68.1% of the total number of common shares outstanding after this offering.

The tables and discussion above do not include:

- 3,864,425 common shares issuable upon exercise of stock options outstanding as of December 31, 2016, at a weighted average exercise price of \$3.61 per share;
- 600,000 common shares issuable upon exercise of warrants outstanding as of December 31, 2016, at an exercise price of \$5.60 per share;
- 1,034,805 common shares reserved and available as of December 31, 2016 for future issuance under our 2014 Equity Incentive Plan, as amended (of which options to purchase an aggregate of 1,034,433 common shares were issued subsequent to December 31, 2016, at a weighted average exercise price of \$10.14 per share); and
- 2,712,741 additional common shares reserved for future issuance under our 2017 Equity Incentive Plan, or the 2017 Plan, and 339,139 common shares reserved for future issuance under our 2017 Employee Share Purchase Plan, or ESPP, each of which became effective upon the signing of the

underwriting agreement related to this offering, as well as any automatic increases in the number of common shares reserved for issuance under the 2017 Plan and the ESPP.

To the extent that stock options or warrants are exercised, new stock options are issued under our equity incentive plan, or we issue additional common shares in the future, there will be further dilution to investors participating in this offering. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our shareholders.

Certain of our existing principal shareholders, directors and their affiliated entities have agreed to purchase an aggregate of 3,142,117 common shares in this offering at the initial public offering price per share. The foregoing discussion and tables do not reflect such purchases by these entities.

# SELECTED CONSOLIDATED FINANCIAL DATA

You should read the following selected consolidated financial data together with our consolidated financial statements and the related notes appearing at the end of this prospectus and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus. We have derived the consolidated statement of operations data for the years ended December 31, 2015 and 2016 and the consolidated balance sheet data as of December 31, 2015 and 2016 from our audited consolidated financial statements appearing at the end of this prospectus. Our historical results are not necessarily indicative of results that may be expected in any future period.

	Year Ended December 31,			
		2015		2016
	(in thousands, exce per share data)			
Consolidated Statement of Operations Data:				
Operating expenses:				
Research and development	\$	7,559	\$	55,529
General and administrative		2,137	_	5,109
Total operating expenses		9,696		60,638
loss from operations		(9,696)		(60,638
Other income (expense):				
Interest expense				(385
Change in fair value of warrant liability		—		154
Change in fair value of derivative liability		(370)		(65
Change in fair value of contingent equity liability		—		(2,263
Loss from equity method investment			_	(247
Total other income (expense), net		(370)		(2,806
loss before provision for income taxes		(10,066)		(63,444
Provision for income taxes				90
Jet loss		(10,066)		(63,534
Less: Net income (loss) attributable to non-controlling interests		(4)		143
Net loss attributable to common shareholders of Biohaven Pharmaceutical				
Holding Company Ltd.	\$	(10,062)	\$	(63,677
Net loss per share attributable to common shareholders of Biohaven				
Pharmaceutical Holding Company Ltd.—basic and diluted <sup>(1)</sup>	\$	(0.91)	\$	(5.05
Veighted average common shares outstanding—basic and diluted <sup>(1)</sup>		11,009		12,608
Pro forma net loss per share attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd.—basic and diluted (unaudited) <sup>(1)</sup>			\$	(4.48
Pro forma weighted average common shares outstanding—basic and diluted (unaudited) <sup>(1)</sup>			-	14,215

(1) See Note 15 to our consolidated financial statements appearing at the end of this prospectus for further details on the calculation of basic and diluted net loss per share attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd. and on the calculation of pro forma basic and diluted net loss per share attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd.

		As of December 31,				
	2015	2016				
	(in the	usands)				
<b>Consolidated Balance Sheet Data:</b>						
Cash	\$ 1,460	\$ 23,565				
Working capital <sup>(1)</sup>	1,558	16,093				
Total assets	1,892	27,017				
Notes payable, net of discount	_	4,216				
Notes payable to related parties	—	595				
Warrant liability	_	780				
Contingent equity liability	—	18,938				
Convertible preferred shares		43,270				
Total shareholders' equity (deficit)	1,087	(45,033)				

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

## 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 the section entitled "Selected Consolidated Financial Data" and our consolidated financial statements and the related notes appearing at the end of this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this prospectus, our actual results could differ materially from the results described in or implied by these forward-looking statements.

### **Overview**

We are a clinical-stage biopharmaceutical company with a portfolio of innovative, late-stage product candidates targeting neurologic diseases, including rare disorders. Our product candidates are small molecules based on two distinct mechanistic platforms—calcitonin gene-related peptide, or CGRP, receptor antagonists and glutamate modulators—which we believe have the potential to significantly alter existing treatment approaches across a diverse set of neurologic indications with high unmet need in both large markets and orphan indications. 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 treatment of migraine. In July 2016, we acquired exclusive, worldwide rights to our CGRP receptor antagonist platform, including rimegepant and another product candidate, BHV-3500, which we are developing for the prevention of chronic and episodic migraine, through a license agreement with Bristol-Myers Squibb Company, or BMS. In 2017, we intend to initiate two Phase 3 clinical trials of rimegepant and to commence IND-enabling studies to allow us to ultimately pursue clinical trials of BHV-3500.

We are developing three product candidates that modulate the body's glutamate system. Two of these product candidates, trigriluzole and BHV-0223, act as glutamate transporter modulators, while our product candidate BHV-5000 is an antagonist of the glutamate *N*-methyl-D-aspartate, or NMDA, receptor. We are developing trigriluzole for the treatment of ataxias, with an initial focus on spinocerebellar ataxia, or SCA. In May 2016, we received orphan drug designation from the U.S. Food and Drug Administration, or FDA, for trigriluzole for the treatment of SCA, and in the fourth quarter of 2016 we enrolled the first patient in a Phase 2/3 clinical trial, from which we expect to report topline results in the first quarter of 2018.

We are developing BHV-0223 for the treatment of amyotrophic lateral sclerosis, or ALS. In December 2016, we received orphan drug designation from the FDA for BHV-0223 to treat ALS. In 2017, we plan to commence a trial comparing the bioequivalence of BHV-0223 and riluzole in healthy volunteers. Depending on the outcome of this bioequivalence study, we plan to file a new drug application, or NDA, with the FDA and pursue the regulatory approval of BHV-0223 for ALS under Section 505(b)(2) of the U.S. Federal Food, Drug, and Cosmetic Act.

We are also developing BHV-5000, an orally available, first-in-class, low-trapping NMDA receptor antagonist, for the treatment of symptoms associated with Rett syndrome, including breathing irregularities. 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, or AstraZeneca, in October 2016. We anticipate completing our commercial-grade formulation efforts for BHV-5000 in the third quarter of 2017. We plan to conduct a Phase 1 clinical trial of BHV-5000 to evaluate its pharmacokinetic properties and then in 2018 to commence a single Phase 2/3 clinical trial of BHV-5000 for the treatment of breathing irregularities associated with Rett syndrome that, if successful, we believe could support our application for regulatory approval.

Since our inception in September 2013, we have devoted substantially all of our resources to organizing and staffing our company, business planning, raising capital, acquiring and developing product candidates and related intellectual property rights, planning for commercialization, and conducting discovery, research and development activities for our product candidates. We do not have any products approved for sale and have not generated any revenue from product sales. We have funded our operations to date primarily with proceeds from the sale of preferred shares and common shares and borrowings under a credit agreement with a bank. Through December 31, 2016, we had received net cash proceeds of \$57.8 million from sales of our preferred shares and common shares and gross proceeds of \$5.0 million from borrowings under the credit agreement. In February 2017, we received net cash proceeds of \$38.6 million from the sale of Series A preferred shares in connection with the second and final closing of our Series A preferred share financing.

Since our inception, we have incurred significant operating losses. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our current product candidates and programs. Our net loss was \$10.1 million and \$63.5 million for the years ended December 31, 2015 and 2016, respectively. As of December 31, 2016, we had an accumulated deficit of \$75.5 million. We expect to continue to incur significant expenses for at least the next several years as we advance our product candidates from discovery through preclinical development and clinical trials and seek regulatory approval and pursue commercialization of any approved product candidate. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. In addition, we may incur expenses in connection with the in-license or acquisition of additional product candidates. Furthermore, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company, including significant legal, accounting, investor relations and other expenses that we did not incur as a private company.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through the sale of equity, debt financings or other capital sources, including collaborations with other companies or other strategic transactions. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back or discontinue the development and commercialization of one or more of our product candidates or delay our pursuit of potential in-licenses or acquisitions.

Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of December 31, 2016, we had cash of \$23.6 million, and in February 2017, we received net cash proceeds of \$38.6 million from the sale of Series A preferred shares in connection with the second and final closing of our Series A preferred share financing. We believe that the anticipated net proceeds from this offering, together with our existing cash, will enable us to repay our indebtedness and to fund our operating expenses and capital expenditure requirements through October 31, 2018. 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."

Without giving effect to the anticipated net proceeds from this offering, we expect that our existing cash will be sufficient to fund our operating expenses, capital expenditure requirements and debt service payments through July 31, 2017. Beyond that point, we will need to raise additional capital to finance our

operations, which cannot be assured. We have concluded that this circumstance raises substantial doubt about our ability to continue as a going concern within one year after the issuance date of our financial statements for the year ended December 31, 2016. See Note 1 to our consolidated financial statements appearing at the end of this prospectus for additional information on our assessment.

Similarly, in its report on our financial statements for the year ended December 31, 2016, our independent registered public accounting firm included an explanatory paragraph stating that our recurring losses from operations since inception and required additional funding to finance our operations raise substantial doubt about our ability to continue as a going concern.

## **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 discovery and development of our product candidates. We expense research and development costs as incurred. These expenses include:

- expenses incurred under agreements with contract research organizations, or CROs, contract manufacturing organizations, or 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, related benefits, travel and share-based compensation expense for employees engaged in research and development functions;
- costs related to compliance with regulatory requirements;
- facilities costs, depreciation and other expenses, which include rent and utilities; and
- 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 information provided to us by our service providers.

Our 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, CMOs, 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 facility expenses, including depreciation 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 discovery as well as for managing our preclinical development, process development, manufacturing and clinical development activities. These employees work across multiple programs and, therefore, we do not track their costs by program.

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The table below summarizes our research and development expenses incurred by program:

		ear Ended ecember 31,
	2015	2016
	(ir	thousands)
BHV-0223	\$ 1,6	27 \$ 380
Rimegepant		- 25,139
Trigriluzole	3,4	97 11,761
BHV-5000		— 13,550
Research and discovery and unallocated costs	2,4	35 4,699
Total research and development expenses	\$ 7,5	59 \$ 55,529

Research and development activities are central to our business model. 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 substantially over the next several years as we increase personnel costs, including share-based compensation, commence Phase 3 clinical trials of rimegepant, continue our ongoing Phase 2/3 clinical trial of trigriluzole, conduct other 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;
- establishing 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;
- establishing 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;
- obtaining, maintaining, defending and enforcing patent claims and other intellectual property rights;
- significant and changing government regulation;
- launching commercial sales of our product candidates, if and when approved, whether alone or in collaboration with others; and
- maintaining a continued acceptable safety profile of the product candidates following approval.

We may never succeed in achieving regulatory approval for any of our product candidates. We may obtain unexpected results from our clinical trials. We may elect to discontinue, delay or modify clinical

trials of some product candidates or focus on others. Any changes in the outcome of any of these variables with respect to the development of our product candidates in preclinical and clinical development could mean a significant change in the costs and timing associated with the development of these product candidates. For example, if the FDA or another regulatory authority were to delay our planned start of clinical trials or require us to conduct clinical trials or other testing beyond those that we currently expect or if we experience significant delays in enrollment in any of our planned clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development of that product candidate. Drug commercialization will take several years and millions of dollars in development costs.

## General and Administrative Expenses

General and administrative expenses consist primarily of salaries, related benefits, travel and 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 headcount to support our continued research activities and development of our product candidates. We also anticipate that we will incur increased accounting, audit, legal, regulatory, compliance, director and officer insurance costs as well as investor and public relations expenses associated with being a public company. We anticipate the additional costs for these services will increase our general and administrative expenses by approximately \$1.5 million to \$2.0 million on an annual basis. Additionally, if and when we believe a regulatory approval of a product candidate appears likely, we anticipate an increase in payroll and expense 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)**

## Interest Expense

Interest expense consists of interest on outstanding borrowings under our credit agreement with Wells Fargo Bank, National Association, or Wells Fargo, entered into in August 2016 at the applicable interest rate as well as amortization of the debt discount relating to that loan. In periods subsequent to December 31, 2016, interest expense will also consist of interest on our notes payable to related parties, which we issued in December 2016 in connection with our acquisition of Biohaven Pharmaceuticals, Inc., or BPI, at the applicable interest rate.

### Change in Fair Value of Warrant Liability

In connection with entering into our credit agreement with Wells Fargo, we agreed to issue warrants to purchase our common shares to the guarantor and co-guarantor of our obligations under the agreement. We classify the warrants as a liability on our consolidated balance sheet that we remeasure to fair value at each reporting date, and we recognize changes in the fair value of the warrant liability as a component of other income (expense), net in our consolidated statement of operations and comprehensive loss. We will continue to recognize changes in the fair value of the warrant liability until the warrants are exercised, expire or qualify for equity classification.

## Change in Fair Value of Derivative Liability

Our license agreement with Yale University, or Yale, provides for a change-of-control payment to Yale upon the occurrence of a change-of-control event, as defined in the agreement, including an initial public offering. We classify the change-of-control payment obligation as a liability on our consolidated balance sheet that we remeasure to fair value at each reporting date, and we recognize changes in the fair value of

the derivative liability as a component of other income (expense), net in our consolidated statement of operations and comprehensive loss. We will continue to recognize changes in the fair value of the derivative liability until a change-of-control event occurs.

## Change in Fair Value of Contingent Equity Liability

Our license agreements with BMS and AstraZeneca require us to issue shares of capital stock upon the occurrence of specified financing or change-of-control events or development milestones, as defined in the agreements. We classify these contingent obligations to issue shares as liabilities on our consolidated balance sheet that we remeasure to fair value at each reporting date, and we recognize changes in the fair values of the contingent equity liabilities as a component of other income (expense), net in our consolidated statement of operations and comprehensive loss. We will continue to recognize changes in the fair values of the contingent equity liabilities until the occurrence of a respective triggering event.

## Loss from Equity Method Investment

In August 2016, we executed a stock purchase agreement with Kleo Pharmaceuticals, Inc., or Kleo, to purchase shares of common stock in an initial closing, with a commitment to purchase additional shares of common stock over a 15-month period through December 2017. As of August 29, 2016 and December 31, 2016, we owned approximately 21.7% and 18.6%, respectively, of the outstanding shares of Kleo. 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.

# **Provision for Income Taxes**

As a company incorporated in the British Virgin Islands, or 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 our losses incurred in the BVI during each reporting period, and no net operating loss carryforwards will be available to us for those losses.

In addition, in each reporting period, our tax provision includes the effects of consolidating the results of operations of BPI, either through December 30, 2016 as a variable interest entity or as of December 31, 2016 as our wholly owned subsidiary. BPI is subject to taxation in the United States. Due to BPI's history of cumulative losses through September 30, 2016, we 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.

During the three months ended December 31, 2016, we fully utilized BPI's remaining U.S. net operating loss carryforwards due to BPI's profitability in that period and we recorded a full release of the valuation allowance, which was an insignificant amount. As a result, we recorded an income tax provision for the first time during the three months ended December 31, 2016.

## Net Income (Loss) Attributable to Non-Controlling Interests

From our inception through December 31, 2016, we consolidated the results of BPI. Although we did not have an ownership interest in BPI during that period, we determined that BPI was a variable interest entity, of which we were the primary beneficiary.

Net income (loss) attributable to non-controlling interests in our consolidated statement of operations and comprehensive loss consists of the portion of the net income or loss of BPI that is not allocated to us. Changes in the amount of net income (loss) attributable to non-controlling interests are directly impacted

by changes in the net income or loss of BPI. On December 31, 2016, we acquired 100% of the issued and outstanding shares of BPI. As a result, for periods subsequent to the acquisition, we no longer report any non-controlling interests related to BPI.

## **Results of Operations**

# Comparison of the Years Ended December 31, 2015 and 2016

The following table summarizes our results of operations for the years ended December 31, 2015 and 2016:

	Year Decem		
	2015	2016	Change
Operating expenses:		(in thousands)	
Research and development	\$ 7,559	\$ 55,529	\$ 47,970
General and administrative	2,137	5,109	2,972
Total operating expenses	9,696	60,638	50,942
Loss from operations	(9,696)		(50,942)
Other income (expense):			
Interest expense		(385)	(385)
Change in fair value of warrant liability		154	154
Change in fair value of derivative liability	(370)	(65)	305
Change in fair value of contingent equity liability		(2,263)	(2,263)
Loss from equity method investment		(247)	(247)
Total other income (expense), net	(370)	(2,806)	(2,436)
Loss before provision for income taxes	(10,066)	(63,444)	(53,378)
Provision for income taxes		90	90
Net loss	(10,066)	(63,534)	(53,468)
Less: Net income (loss) attributable to non-controlling interests	(4)	143	147
Net loss attributable to common shareholders of Biohaven			
Pharmaceutical Holding Company Ltd.	\$ (10,062)	\$ (63,677)	\$ (53,615)

# Research and Development Expenses

	Year Ended December 31,					
	2015 2016		Change			
			(in	thousands	) —	
Direct research and development expenses by program:						
BHV-0223	\$	1,627	\$	380	\$	(1,247)
Rimegepant				25,139		25,139
Trigriluzole		3,497		11,761		8,264
BHV-5000				13,550		13,550
Research and discovery and unallocated costs:						
Personnel related (including share-based compensation)		1,915		4,137		2,222
Other		520		562		42
Total research and development expenses	\$	7,559	\$	55,529	\$	47,970

Research and development expenses were \$7.6 million for the year ended December 31, 2015, compared to \$55.5 million for the year ended December 31, 2016. The increase of \$48.0 million was primarily due to increases of \$25.1 million in direct costs for our rimegepant program, \$13.6 million in direct costs for our BHV-5000 program, \$8.3 million in spending related to our trigriluzole program and \$2.3 million in research and discovery and unallocated costs, all partially offset by a decrease of \$1.2 million in direct costs for our BHV-0223 program.

The increase in direct costs for our rimegepant program was primarily due to an accrual of a liability of \$13.1 million for our contingent obligation to issue equity to BMS under our license agreement with BMS and the payment of \$9.0 million in license fees under that agreement. The increase in direct costs for our BHV-5000 program was due to an accrual of a liability of \$8.6 million for our contingent obligation to issue equity to AstraZeneca under our license agreement and the payment of \$5.0 million in license fees under that agreement. The increase in direct costs for our trigriluzole program primarily related to an animal toxicity study that commenced in December 2015.

The increase in research and discovery and unallocated costs was primarily due to an increase of \$2.2 million in personnel-related costs, including share-based compensation, as a result of hiring additional personnel in our research and development department. Personnel-related costs for the year ended December 31, 2015 and 2016 included share-based compensation expense of \$1.5 million and \$2.4 million, respectively.

The decrease in direct costs for our BHV-0223 program was due to formulation work and Phase 1 clinical trial work that was completed during the year ended December 31, 2015. Our Phase 2 clinical trial of BHV-0223 had not begun as of December 31, 2016.

## General and Administrative Expenses

General and administrative expenses were \$2.1 million for the year ended December 31, 2015, compared to \$5.1 million for the year ended December 31, 2016. The increase of \$3.0 million was primarily due to increases of \$1.9 million in personnel-related costs, including share-based compensation, \$1.0 million in professional fees and \$0.1 million in facility-related costs. Personnel-related costs for the year ended December 31, 2015 and 2016 included share-based compensation expense of \$1.3 million and \$2.2 million, respectively. The increase in personnel-related costs was due to the hiring of additional personnel in our general and administrative functions. Professional fees increased due to costs associated with the preparation, audit and review of our financial statements as well as ongoing business operations.

#### Other Income (Expense), Net

Other income (expense), net was a net expense of \$0.4 million for the year ended December 31, 2015, compared to \$2.8 million for the year ended December 31, 2016. The increase of \$2.4 million in net expense was primarily due to an increase of \$2.3 million in the fair value of the contingent equity liability associated with our license agreements with BMS and AstraZeneca and an increase in interest expense of \$0.4 million due to interest on borrowings under our credit agreement with Wells Fargo that we entered into in August 2016. These increases in other expense were partially offset by a decrease of \$0.3 million in the change in the fair value of the derivative liability associated with Yale.

#### Provision for Income Taxes

We recorded no provision for income taxes for the year ended December 31, 2015, compared to a provision of \$0.1 million for the year ended December 31, 2016. We recorded a tax provision in 2016 for the U.S. federal and state income taxes of BPI's profitable operations in the United States and due to the fact that, in the three months ended December 31, 2016, we fully utilized BPI's remaining U.S. net operating loss carryforwards.

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## **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. We have funded our operations to date primarily with proceeds from the sale of preferred shares and common shares and borrowings under our credit agreement with Wells Fargo. Through December 31, 2016, we had received net cash proceeds of \$57.8 million from sales of our preferred shares and common shares and gross proceeds of \$5.0 million from borrowings under the credit agreement. As of December 31, 2016, we had cash of \$23.6 million. In February 2017, we received net cash proceeds of \$38.6 million from the sale of Series A preferred shares in connection with the second and final closing of our Series A preferred share financing.

Cash in excess of immediate requirements is invested primarily with a view to liquidity and capital preservation.

## **Cash Flows**

The following table summarizes our cash flows for each of the periods presented:

	Year E Decemb	
	2015	2016
	(in thou	sands)
Net cash used in operating activities	\$ (5,625)	\$ (29,504)
Net cash used in investing activities	(3)	(3,153)
Net cash provided by financing activities	5,316	54,762
Net increase (decrease) in cash	\$ (312)	\$ 22,105

## **Operating** Activities

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 increases in accrued expenses and accounts payable were primarily due to increases in clinical trial costs and professional fees associated with the preparation, audit and review of our financial statements.

During the year ended December 31, 2015, operating activities used \$5.6 million of cash, resulting from our net loss of \$10.1 million and net cash used in changes in our operating assets and liabilities of \$0.3 million, partially offset by non-cash charges of \$4.7 million. Net cash used in changes in our operating assets and liabilities for the year ended December 31, 2015 consisted primarily of a \$0.4 million increase in prepaid expenses and other current assets as a result of prepayments under our ongoing research, development and clinical trial work performed by CROs, partially offset by a \$0.1 million increase in accrued expenses. The increase in accrued expenses 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, 2016, we used \$3.2 million of cash in investing activities, primarily consisting of our investment in Kleo.

During the year ended December 31, 2015, we used an insignificant amount of cash in investing activities, consisting of purchases of property and equipment.

## Financing Activities

During the year ended December 31, 2016, net cash provided by financing activities was \$54.8 million, primarily consisting of net cash proceeds of \$38.6 million from our issuance of Series A preferred shares in October 2016, net cash proceeds of \$11.3 million from our issuance of common shares and gross proceeds of \$5.0 million from borrowings under the credit agreement, partially offset by \$0.2 million of payments of debt issuance costs associated with the borrowings.

During the year ended December 31, 2015, net cash provided by financing activities was \$5.3 million, consisting of net proceeds of \$4.8 million from our issuance of common shares and net proceeds of \$0.5 million from the collection of a note receivable from Portage Biotech, Inc. in connection with its initial equity investment in our company.

## **Credit Agreement**

On August 30, 2016, we entered into a one-year credit agreement with Wells Fargo providing for a term loan in the principal amount of \$5.0 million, or the Credit Agreement, and we borrowed the full \$5.0 million available. Our obligations under the Credit Agreement are guaranteed by a member of our board of directors, who is also a shareholder. A second member of our board of directors and shareholder agreed to serve as a secondary guarantor for 50% of the loan balance. In connection with their guaranties of the loan, we issued to each director an immediately exercisable warrant to purchase 107,500 common shares at an exercise price of \$9.2911 per share. Borrowings under the Credit Agreement bear interest at a variable rate equal to monthly LIBOR, which was 0.77% as of December 31, 2016, plus 1.50% per annum. In the event of a default, the interest rate applicable is equal to the monthly LIBOR rate then in effect, increased by 4.0% per annum. The Credit Agreement requires monthly, interest-only payments through the maturity date of August 30, 2017, at which date all remaining amounts will be due and payable. The Credit Agreement contains affirmative and negative covenants, but does not contain any financial covenants.

## Notes Payable to Related Parties

On December 31, 2016, we 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 \$0.6 million. We funded the acquisition through the issuance of promissory notes to each of the former stockholders of BPI. The former beneficial stockholders of BPI are shareholders of our company and currently serve as our chief executive officer, our chief medical officer and the chairman of our board of directors, respectively. The notes are payable in five annual payments, the first four of which are interest only, with the final payment to include the principal balance outstanding plus any accrued and unpaid interest. The notes bear interest at a rate of 4.5% per annum and mature on December 31, 2021. The notes become immediately due and payable upon specified events, including immediately prior to the consummation of this offering or upon the occurrence of a change of control of our company. There are no affirmative, negative or financial covenants associated with the notes.

## **Funding Requirements**

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the preclinical activities and clinical trials of our product candidates. In addition, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. Our expenses will also increase as we:

- initiate our two planned Phase 3 clinical trials of rimegepant, conduct our ongoing Phase 2/3 potentially pivotal trial of trigriluzole and complete our planned bioequivalence study for BHV-0223;
- initiate 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;

- support formulation efforts of BHV-5000 and initiate our planned Phase 1 clinical trial for that product candidate;
- initiate formulation and clinical development for BHV-3500;
- complete commercial-grade formulation work and stability testing for all our programs;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure in anticipation of commercializing any product candidates for which we may obtain marketing approval and intend to commercialize on our own or jointly;
- hire additional clinical, medical, and development personnel;
- expand our infrastructure and facilities to accommodate our growing employee base;
- transition our organization to being a public company;
- maintain, expand and protect our intellectual property portfolio; and
- acquire or in-license other product candidates and technologies.

We believe that the anticipated net proceeds from this offering, together with our existing cash, will enable us to repay our indebtedness and to fund our operating expenses and capital expenditure requirements through October 31, 2018, including the completion of our ongoing Phase 2/3 clinical trial of trigriluzole. 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, trigriluzole or our other product candidates, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution, depending on where we choose to commercialize.

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 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 equity offerings, debt financings, collaboration agreements, 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, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common shareholder. 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, collaborations agreements, 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 may 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, 2016 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		to 5 (ears		ore than Years
				(i	n th	ousands)						
Research commitments <sup>(1)</sup>	\$	6,973	\$	5,154	\$	1,819	\$		\$			
Debt obligations <sup>(2)</sup>		5,836		5,133		54		649		_		
Share purchase obligations <sup>(3)</sup>		5,750		5,750								
Total	\$	18,559	\$	16,037	\$	1,873	\$	649	\$			

<sup>(1)</sup> 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.

- (2) Amounts in the table reflect the contractually required principal and interest payable pursuant to outstanding borrowings under the Credit Agreement and notes payable to related parties. Interest payments due under the Credit Agreement in the table above were calculated using an interest rate of 2.27%, which was the interest rate applicable to borrowings under the Credit Agreement as of December 31, 2016.
- (3) Amounts in the table reflect the cash portion of our commitments to purchase an aggregate of 5,500,000 shares of common stock of Kleo through December 2017 and to purchase 500,000 shares of Kleo common stock from an officer and stockholder of Kleo in January 2017. In March 2017, we purchased the 500,000 shares of Kleo common stock for consideration consisting of \$249,750 in cash and 32,500 of our common shares and we purchased 1,375,000 shares of Kleo common stock for cash consideration of \$1.4 million pursuant to our commitment.

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.

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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.

Under our license agreement with BMS, we are obligated to make development milestone payments of up to \$127.5 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, 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 MGH, we are obligated to pay an annual license maintenance fee of up to \$50,000, 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 and 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 \$25,000 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 \$0.1 million per year.

### **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. 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 Note 2 to our consolidated financial statements appearing at the end of this prospectus, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated 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 advanced 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 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.

# **Share-Based** Compensation

We measure stock options and other share-based awards granted to employees and directors based on the fair value on the date of the grant and recognize the corresponding 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.

For share-based awards granted to consultants and non-employees, we recognize compensation expense over the period during which services are 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 is 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.

#### Determination of the Fair Value of Common Shares

As there has been no public market for our common shares to date, the estimated fair value of our common shares has been determined by our board of directors as of the date of each option grant, with input from management, considering our most recent arm's-length sale of our common shares or third-party valuation of our common shares as well as our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent sale of our common shares or third-party valuation through the date of the grant. Our board of directors considered various objective and subjective factors to determine the fair value of our common shares as of each grant date, including:

- the prices at which we sold preferred shares and the superior rights and preferences of the preferred shares relative to our common shares at the time of each grant;
- the progress of our research and development programs, including the status of preclinical studies and planned clinical trials for our product candidates;
- our stage of development and commercialization and our business strategy;
- external market conditions affecting the biotechnology industry, and trends within the biotechnology industry;
- our financial position, including cash on hand, and our historical and forecasted performance and operating results;
- the lack of an active public market for our common shares and our preferred shares;
- the likelihood of achieving a liquidity event, such as an initial public offering, or IPO, or a sale of our company in light of prevailing market conditions; and
- the analysis of IPOs and the market performance of similar companies in the biopharmaceutical industry.

In the course of preparing for this offering, in February 2017, we obtained third-party valuations, performed on a retrospective basis, of our common shares as of August 17, 2015, the date we issued common shares and common share warrants in connection with our license agreement with ALS Biopharma, and as of October 31, 2016, the date of the first closing of our Series A preferred share financing. In addition, we obtained third-party valuations of our common shares as of various dates between December 31, 2016 and March 31, 2017. Our third-party valuations resulted in valuations of our common shares of \$5.23 per share as of August 17, 2015, \$6.73 per share as of October 31, 2016, \$7.45 per share as of December 31, 2016, \$8.68 per share as of January 31, 2017, \$9.85 per share as of February 28, 2017 and \$10.82 per share as of March 31, 2017. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*.

Our third-party valuation of common shares performed as of August 17, 2015 was prepared using the discounted cash flow, or DCF, method, a form of the income approach, to estimate our equity value. In

order to estimate equity value, the DCF method uses the estimated present value of future net cash flows for the expected life of the related assets or business, discounted at a rate of return that considers the relative risk of achieving those cash flows, the time value of money and the current stage of development of the business. A reasonable discount for lack of marketability is applied to the total equity value to arrive at an estimate of the total fair value of equity on a non-marketable basis. The total fair value of equity on a non-marketable basis is then allocated between each class of equity, including common shares, stock options and warrants. The aggregate fair value of outstanding options and warrants, which was calculated using the Black-Scholes option-pricing model, was deducted from the total equity value on a non-marketable basis to arrive at the fair value of common shares outstanding.

Our third-party valuations of common shares performed as of every other date listed above were prepared using the hybrid method, which used market approaches to estimate our enterprise value. The hybrid method is a probability-weighted expected return method, or PWERM, where the equity value in one or more of the scenarios is calculated using an option-pricing method, or OPM. The OPM treats common shares and preferred shares as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common shares have value only if the funds available for distribution to shareholders exceeded the value of the preferred share liquidation preferences at the time of the liquidity event, such as a strategic sale or a merger. The PWERM is a scenario-based methodology that estimates the fair value of common shares based upon an analysis of future values for the company, assuming various outcomes. The common share value is based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each class of shares. The future value of the common shares under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common shares.

The assumptions underlying these valuations represent management's best estimates, which involve inherent uncertainties and the application of management judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our share-based compensation expense could be materially different.

Following the closing of this offering, the fair value of our common shares will be determined based on the quoted market price of our common shares.

# **Options Granted**

The following table sets forth by grant date the number of shares subject to options granted between January 1, 2015 and April 6, 2017, the per share exercise price of the options, the fair value of common shares per share on each grant date, and the per share estimated fair value of the options:

Grant Date	Number of Shares Subject to Options Granted		er Share Exercise Price of Options	pe	air Value r Common Share on rant Date	Per Share Estimated Fair Value of Options		
October 23, 2015	1,247,500	\$	5.60	\$	5.23	\$	3.22	
December 15, 2016	616,925	\$	9.29	\$	6.73	\$	4.09	
January 9, 2017	5,500	\$	9.29	\$	7.45	\$	4.24	
January 11, 2017	54,000	\$	9.29	\$	7.45	\$	4.41	
January 25, 2017	10,800	\$	9.29	\$	8.68	\$	5.12	
January 31, 2017	325,819	\$	9.29	\$	8.68	\$	5.44	
February 15, 2017	20,800	\$	9.29	\$	8.68	\$	5.15	
February 27, 2017	54,000	\$	9.85	\$	9.85	\$	5.94	
March 6, 2017	10,000	\$	9.85	\$	9.85	\$	6.01	
April 5, 2017	74,000	\$	10.82	\$	10.82	\$	6.84	
April 6, 2017	479,514	\$	10.82	\$	10.82	\$	7.03	

## Valuation of Warrant Liability

In connection with entering into the Credit Agreement, we agreed to issue warrants to purchase our common shares to the guarantor and co-guarantor of our obligations under the agreement. We classify the warrants as a liability on our consolidated balance sheet because each warrant represents a freestanding financial instrument that it not indexed to our 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. We will continue to recognize changes in the fair value of the warrant liability until the warrants are exercised, expire or qualify for equity classification.

We utilize 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 future expected share prices, to value our warrant liability. The Monte Carlo simulation incorporates assumptions and estimates to value the warrant liability. We assess these assumptions and estimates on a quarterly basis as additional information impacting the assumptions is obtained. Estimates and assumptions impacting the fair value measurement include the estimated probability of adjusting the exercise price of the warrants, the number of shares for which the warrants are exercisable, the fair value per share of the underlying common shares issuable upon exercise of the warrants, remaining contractual term of the warrants, risk-free interest rate, expected dividend yield and expected volatility of the price of the underlying common shares. We estimated the fair value of our common shares by taking into consideration the most recent arm's-length sale of our common shares or third-party valuation of our shares. Therefore, we estimate 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 is 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 we have never paid or declared dividends and do not intend to do so in the foreseeable future.

#### Valuation of Derivative Liability

Our license agreement with Yale provides 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. We classify the change-of-control payment obligation as a liability on our consolidated balance sheet because it represents a contingent obligation to pay a variable amount of cash that may be based, in part, on the value of our own shares. The derivative liability was initially recorded at fair value upon entering into the license agreement and is subsequently remeasured to fair value at each reporting date. Changes in the fair value of the derivative liability are recognized as a component of other income (expense), net in our consolidated statement of operations and comprehensive loss. We will continue to recognize changes in the fair value of the derivative liability until a change-of-control event occurs.

The fair value of the derivative liability was determined using the PWERM, which considers as inputs the type and probability of occurrence of a change-of-control event, the amount of the payment, the expected timing of a change-of-control event and a risk-adjusted discount rate. The estimates are based, in part, on subjective assumptions and could differ materially in the future. Changes to these assumptions could have a significant impact on the fair value of the derivative liability.

## Valuation of Contingent Equity Liability

Our license agreements with BMS and AstraZeneca require us to issue shares of capital stock upon the occurrence of specified financing or change-of-control events or development milestones, as defined in

the agreements. In each agreement, the class and number of shares to be issued upon a triggering event were not known upon entering into the license agreements; however, the dollar amount of the shares to be issued upon a triggering event is fixed. We classify these contingent obligations to issue shares as a liability on our consolidated balance sheet because each represents an obligation to issue a variable number of shares for a fixed dollar amount. Each contingent equity liability was initially recorded at fair value upon entering into each respective agreement and is subsequently remeasured to fair value at each reporting date. Changes in the fair values of the contingent equity liabilities are recognized as a component of other income (expense), net in our consolidated statement of operations and comprehensive loss. We will continue to recognize changes in the fair values of the contingent equity liabilities until the occurrence of a respective triggering event.

The fair values of the contingent equity liabilities were determined using the PWERM, which considers as inputs the probability of occurrence of events that would trigger the issuance of shares, the expected timing of such events, the expected value of the contingently issuable equity upon the occurrence of a triggering event and a risk-adjusted discount rate. The estimates are based, in part, on subjective assumptions and could differ materially in the future. Changes to these assumptions could have a significant impact on the fair value of the contingent equity liabilities.

In October 2016, upon the initial closing of our Series A preferred share financing, we issued to AstraZeneca 538,150 Series A preferred shares in partial satisfaction of our obligation to issue shares under our license agreement with AstraZeneca. In connection with this offering, we expect that we will issue an aggregate of 1,883,523 additional common shares to BMS and AstraZeneca in satisfaction of our remaining obligation to issue shares under our license agreements with BMS and AstraZeneca. As a result, upon the closing of this offering, the then-current fair value of the contingent equity liabilities will be reclassified to shareholders' equity and the contingent equity liabilities will no longer be outstanding.

## **Emerging Growth Company Status**

The Jumpstart Our Business Startups Act of 2012 permits an "emerging growth company" such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have irrevocably elected to "opt out" of this provision and, as a result, we will comply with new or revised accounting standards when they are required to be adopted by public companies that are not emerging growth companies.

## **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 Securities and Exchange Commission.

#### **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 prospectus.

## Quantitative and Qualitative Disclosures about Market Risks

#### Interest Rate Risk

As of December 31, 2016, we had \$5.0 million of borrowings outstanding under the Credit Agreement. Amounts outstanding under the Credit Agreement bear interest at a variable rate equal to monthly LIBOR, which was 0.77% as of December 31, 2016, plus a margin of 1.50%. An immediate 10% change in monthly LIBOR rates would not have had a material impact on our debt-related obligations, financial position or results of operations. In addition, given the short-term nature of the Credit Agreement, which matures in August 2017, we do not believe our exposure to interest rate risk is significant.

Our notes payable to related parties outstanding as of December 31, 2016 bear interest at fixed interest rates and, therefore, do not expose us to interest rate risk.

# BUSINESS

# 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 two distinct mechanistic platforms—calcitonin gene-related peptide, or CGRP, receptor antagonists and glutamate modulators—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 markets and orphan indications. The most advanced product candidate from our CGRP receptor antagonist platform is rimegepant, which we are developing for the acute treatment of migraine and for which we intend to initiate two Phase 3 clinical trials in the second half of 2017, with topline results expected in the first quarter of 2018. The most advanced product candidate from our glutamate modulation platform is trigriluzole, which we are developing for the treatment of atxias with an initial focus on spinocerebellar ataxia, or SCA. We have received orphan drug designation from the FDA for trigriluzole in SCA, and we began a Phase 2/3 clinical trial in SCA in December 2016 and expect to report topline results in the first quarter of 2018. Our second most advanced product candidate from our glutamate modulation platform is BHV-0223, which we are developing for the treatment of amyotrophic lateral sclerosis, or ALS, a neurodegenerative disease that affects nerve cells in the brain and spinal cord. We have received orphan drug designation from the FDA for BHV-0223 in ALS.

We believe many of our product candidates have the potential to be first-in-class or best-in-class treatment options, while others will potentially represent the first available treatment options for their indications. Based on the data from its Phase 2b clinical trial, we believe rimegepant has the potential to be the best-in-class CGRP receptor antagonist for the acute treatment of migraine, having shown statistically significant improvement on the symptoms of pain, nausea, photophobia and phonophobia associated with migraine attacks. To our knowledge, rimegepant is the only small molecule CGRP receptor antagonist currently in development for the acute treatment of migraine to have achieved statistical significance, meaning there is a low probability, typically less than 5%, that the difference happened by chance, on all of these measures in a single study. We also believe that trigriluzole has the potential to be the first FDA-approved drug treatment option for ataxias. We intend to expedite development of trigriluzole for SCA using the Section 505(b)(2) regulatory pathway and are currently conducting a Phase 2/3 trial that we believe, if successful, may be sufficient to support our application for regulatory approval of trigriluzole. We believe that BHV-0223 has the potential to be the first-in-class sublingual treatment for ALS. BHV-0223 is designed to deliver the unique pharmacologic, glutamate modulation effects of riluzole which has shown a survival benefit for ALS patients, and which is currently the only treatment for ALS approved by the FDA. We believe BHV-0223 could also provide best-in-class formulation attributes such as ease of administration, more predictable pharmacokinetic performance, no food effect, reduced drug load and reduced liver exposure.

### Our CGRP Receptor Antagonist Platform: Rimegepant and BHV-3500 Targeting Migraine

Our CGRP receptor antagonist platform comprises two product candidates: rimegepant for the acute treatment of migraine and BHV-3500 for the prevention of chronic and episodic migraine. Rimegepant, the lead product candidate, is an orally available, selective and potent small molecule CGRP receptor antagonist. 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 2010 rates migraine as the seventh highest specific cause of disability worldwide. According to the American Migraine Foundation, migraine affects approximately 36 million people in the United States, and treatment of migraine accounted for an estimated market of approximately \$1.9 billion in 2012 in the United States. Current treatment approaches, such as triptans, can be limited by headache recurrence, which are headaches that are relieved and then reoccur within 24 hours after taking migraine medication, and cardiovascular contraindications or warnings. We believe rimegepant has the potential to be a best-in-class

CGRP receptor antagonist for the acute treatment of migraine with the ability to address important unmet needs, such as durable efficacy across all four traditional migraine symptoms and reduced incidence of headache recurrence, without contraindications or warnings in patients with cardiovascular disease or hypertension, since its CGRP-based mechanism of action does not involve active vasoconstriction, or the constriction of blood vessels.

In a Phase 2b, double-blind, randomized, placebo-controlled, dose-ranging clinical trial of 812 patients completed by Bristol-Myers Squibb Company, or BMS, rimegepant dosed at 75 mg was observed to have statistically significant improvement as compared to placebo on all four key migraine symptoms-pain, nausea, photophobia and phonophobia-the four traditional endpoints identified by the U.S. Food and Drug Administration, or FDA, for drug approval for treatment of migraine. To our knowledge based on publicly available information, rimegepant is the only small molecule CGRP receptor antagonist currently in development that has achieved statistically significant improvement on all four of the traditional endpoints within a single study. Rimegepant also was observed to have statistically significant effects on two-to-24 hour and two-to-48 hour pain freedom (head pain intensity level reported as "no pain") and two-to-24 hour pain relief (no pain or mild pain), as compared to placebo. In these measurements, benefits were present at two hours after dosing and persisted through 24 hours after dosing and, with respect to pain freedom, persisted through 48 hours after dosing. This durable improvement is significant because other common migraine medications, such as triptans, have been linked to the headache recurrence. The Phase 2b data also showed statistically significant improvement as compared to placebo in multiple doses of rimegepant. As of December 31, 2016, approximately 687 subjects have received single or multiple doses of rimegepant, and no treatment-related serious adverse events have been observed and adverse events have generally been mild and transient in nature. In the second half of 2017, we plan to commence two Phase 3 clinical trials of rimegepant for the acute treatment of migraine, with topline results expected in the first quarter of 2018. We are advancing the 75 mg dose of rimegepant in our Phase 3 clinical trials, as that dose was the lowest effective dose in the Phase 2b trial and there did not appear to be additional benefits of higher doses, which is a general characteristic of the doseresponse profile of acute treatments for migraine.

BHV-3500, the second product candidate from our CGRP receptor antagonist platform, is a small molecule, structurally distinct from rimegepant, that we are developing for the prevention of chronic and episodic migraine. Chronic migraine is characterized by experiencing 15 or more headache days per month, while episodic migraine is characterized by experiencing fewer than 15 headache days per month. BHV-3500 is potent, highly soluble and selective at the human CGRP receptor. In addition, BHV-3500 has demonstrated in nonclinical studies characteristics that we believe will make it particularly well suited for daily preventative treatment of chronic and episodic migraine. Preliminary proof-of-concept has been observed in a marmoset model with oral delivery and, based on preliminary preclinical evaluations, no significant cardiovascular safety or systemic toxicity issues have been observed. We believe BHV-3500's chemical properties also make the product candidate potentially suitable for multiple routes of delivery, including nasal, subcutaneous, inhalation or oral administration. Because BHV-3500 has exhibited an efficacy profile similar to rimegepant in preclinical studies, we believe that BHV-3500 may demonstrate similar comprehensive and durable improvements in the four key migraine symptoms. In 2017, we plan to commence studies to enable an investigational new drug application, or IND, to ultimately pursue clinical trials of BHV-3500 for the prevention of chronic and episodic migraine.

We acquired exclusive, worldwide rights to our CGRP receptor antagonist platform, including rimegepant and BHV-3500, through a license agreement with BMS. As part of this agreement, BMS has taken an equity stake in our company.

### Our Glutamate Modulation Platform: Trigriluzole, BHV-0223 and BHV-5000 Targeting Orphan Neurological Indications

Under our glutamate modulation platform, we are currently developing three product candidates, trigriluzole (previously known as BHV-4157) for the treatment of ataxias, BHV-0223 for the treatment of ALS and BHV-5000 for the treatment of symptoms associated with Rett syndrome, including breathing irregularities. These product candidates modulate the glutamate system via two distinct mechanisms—glutamate transporter modulation (trigriluzole and BHV-0223) and glutamate *N*-methyl-D-aspartate, or NMDA, receptor antagonism (BHV-5000).

Trigriluzole is a third-generation tripeptide prodrug, that converts to the active metabolite riluzole, that we are developing for the treatment of ataxias. We believe that trigriluzole will qualify as a new chemical entity, or NCE, if it receives regulatory approval by the FDA. Trigriluzole has the potential to be the first drug approved by the FDA for the treatment of ataxias, and we have chosen SCA as our lead indication. SCA is one of a group of rare genetic disorders that is characterized by slowly progressive incoordination of gait, speech and hand and eye movements. In general, a person with SCA retains full mental capacity but progressively loses physical control over voluntary muscles. 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. Other ataxias affect an aggregate of greater than 100,000 individuals in the United States. No approved drug treatments for SCA are currently available. We believe that trigriluzole may be effective in the treatment of SCA based on the results of two prior randomized controlled trials conducted by third parties, in which riluzole was observed to have statistically significant improvements in ataxia-related endpoints, and the results of multiple in vivo and in vitro preclinical studies that suggest that trigriluzole may mitigate the limitations of riluzole. In May 2016, we received orphan drug designation from the FDA for trigriluzole in SCA, and we intend to develop trigriluzole for SCA under Section 505(b)(2) of the U.S. Federal Food, Drug, and Cosmetic Act. Trigriluzole had been dosed in 58 subjects in a Phase 1 clinical trial and has been generally well tolerated, without evidence of novel, clinically significant safety signals or lab abnormalities compared to the active metabolite riluzole. We are currently enrolling in our Phase 2/3 clinical trial, which 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, which we believe, if successful, may be sufficient to support our application for regulatory approval of trigriluzole. We enrolled the first patient in our Phase 2/3 clinical trial in December 2016, and we expect to report topline results from this trial in the first quarter of 2018. If the results of this trial are positive, we anticipate submitting a new drug application, or NDA, to the FDA in 2018.

BHV-0223 is a sublingual, oral disintegrating tablet, or ODT, formulation of riluzole that we are developing for the treatment of ALS. ALS is a progressive neurodegenerative motor neuron disease that affects nerve cells in the brain and the spinal cord. 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. Orally administered riluzole, which was approved by the FDA in 1995, remains the only agent shown to extend survival and time to tracheostomy in patients with ALS, although it has significant shortcomings that limit its utility. We believe that BHV-0223 has the potential to significantly improve the treatment of patients with ALS by combining the unique pharmacologic activities of glutamate modulation that are conferred by riluzole with an improved pharmacologic profile that results in easier administration, more predictable pharmacokinetic performance, no food effect, reduced drug load and reduced liver exposure compared to oral riluzole. In December 2016, we received orphan drug designation from the FDA for BHV-0223 in ALS. BHV-0223 had been dosed in 11 subjects as of January 31, 2017 in connection with our Phase 1 clinical trial. Adverse events have generally been mild and transient, and no treatment-related serious adverse events have been observed. In 2017, we plan to commence a bioequivalence study of BHV-0223 40 mg to riluzole 50 mg in healthy volunteers. We plan to subsequently submit an NDA for the use of BHV-0223 in patients with ALS and pursue regulatory approval under the Section 505(b)(2) regulatory pathway.

BHV-5000 is an orally available, first-in-class, low-trapping, NMDA receptor antagonist prodrug that we are developing for the treatment of symptoms associated with Rett syndrome, including breathing irregularities. 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. As a low-trapping NMDA receptor antagonist, BHV-5000 has differentiating pharmacologic properties compared to other agents that have been in development within this drug class. The unique property of a low-trapping NMDA receptor antagonist is its ability to uncouple from the target receptor more freely, a property that is thought to mitigate the dissociative or psychotic-like effects that have been observed with other NMDA antagonists. We are studying BHV-5000 in Rett syndrome based on results of ketamine studies 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. We anticipate completing our commercial-grade formulation for BHV-5000 in the third quarter of 2017. As of December 31, 2016, BHV-5000 had been dosed in approximately 40 healthy subjects in a Phase 1 trial conducted by AstraZeneca AB, or AstraZeneca, and has been observed to be well tolerated with no clinically relevant safety signals. Its active metabolite, lanicemine, has been administered in clinical trials conducted by AstraZeneca to approximately 790 subjects, in single or multiple doses, and has been observed to be generally well tolerated with most adverse events being mild and transient in nature. After a confirmatory Phase 1 clinical trial, which we plan to initiate in 2017, to bridge pharmacokinetics with a prior formulation, we plan to commence a single Phase 2/3 clinical trial of BHV-5000 for the treatment of breathing irregularities associated with Rett syndrome in 2018, with the potential for this to be a pivotal trial that, if successful, we believe could support our application for regulatory approval.

We acquired exclusive, worldwide rights to BHV-5000 through a license agreement with AstraZeneca in October 2016. As part of this agreement, AstraZeneca has taken an equity stake in our company.

In addition to ataxias, ALS and Rett syndrome, we may expand our pipeline into other therapeutic indications where glutamate plays a central role in the pathophysiology of the disease, including anxiety and mood disorders.

# **Biohaven Management Team**

We are led by a team of experienced executives who have held senior research and development positions at leading biotech and large pharmaceutical companies. Members of our management team and board of directors have deep experience leading neuroscience research and have been involved in the development and commercialization of numerous drugs, such as Zoloft, Abilify, Opdivo, Yervoy and Soliris. This depth of experience has facilitated our ability to license important product candidates and intellectual property from top-tier pharmaceutical companies and leading academic institutions, such as AstraZeneca, BMS, ALS Biopharma, Rutgers University, the Massachusetts General Hospital (a teaching hospital of Harvard Medical School) and Yale University. Members of our Scientific Advisory Board hold or have held affiliations with Yale University, Harvard Medical School, the National Institutes of Health and the FDA. We also have ongoing academic collaborations with Johns Hopkins University, Columbia University, Rutgers University and Yale University. We believe the strength of our management team and board of directors positions us well to enter into additional license and collaboration arrangements with world-class institutions and large pharmaceutical companies.

# **Product Candidates**

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

Product Candidate		Preclinical Phase 1 Phase 2			Phase 3	Last Event	Next Expected Event		
Rimegepant		Acute Treatment of Mig	graine	>		Positive Phase 2b	Commence two Phase 3 trials in 2017; topline results expected 1Q 2018		
Plat	BHV-3500	Prevention of Chronic and Episodic Migraine	>			Preclinical studies File IND with FDA in			
	Trigriluzole	Spinocerebellar Ataxia	(SCA)			First patient enrolled in Phase 2/3 trial in Q4 2016	Phase 2/3 topline results in 1Q 2018		
F		Friedreich's Ataxia							
Platform		Sporadic Ataxia		8					
Glutamate	BHV-0223	Amyotrophic Lateral S (ALS)	clerosis	i.		Phase 1	Commence bioequivalence study in 2017; submit NDA in 2018		
0		Rett Syndrome				In-licensed from AstraZeneca	Commence Phase 1 pharmacokinetic trial in 2017		
	BHV-5000	Other Neuropsychiatric Indications				In-licensed from AstraZeneca			

### **Our Strategy**

Our goal is to become a leader in the development of innovative therapies for neurological diseases that have the potential to change current treatment paradigms. The key elements of our strategy to achieve this goal include:

- **Rapidly advance and commercialize our portfolio of migraine product candidates.** We believe our novel small molecule, orally available CGRP receptor antagonists, rimegepant and BHV-3500, have the potential to be best-in-class treatments for migraine. Rimegepant was observed to have statistically significant improvement, as compared to placebo, on migraine pain and associated symptoms of nausea, phonophobia and photophobia in a Phase 2b trial of acute treatment of migraine. In the second half of 2017, we expect to initiate two Phase 3 clinical trials with rimegepant for the acute treatment of migraine, with topline results expected in the first quarter of 2018. We are also planning a 12-month, long-term safety study of rimegepant to meet FDA requirements for approval. We are designing our Phase 3 development program to support regulatory approval in the United States, as well as to support regulatory filings in Europe and Japan. We plan to complete IND-enabling studies to begin human testing with BHV-3500 in 2017 and to subsequently pursue an indication for the prevention of chronic and episodic migraine. We also intend to explore multiple formulations, such as intranasal, inhalation, subcutaneous or oral routes of administration, with BHV-3500.
- Complete the development and commercialization of our novel glutamate modulator trigriluzole as potentially the first FDA-approved drug treatment for patients suffering from ataxias. Following our receipt of FDA orphan drug designation for trigriluzole in May 2016, and our IND becoming effective in 2016, we initiated a Phase 2/3 clinical trial for the treatment of SCA and enrolled the first patient in this trial in December 2016. We believe this trial, if successful, may be sufficient to support our application for regulatory approval of trigriluzole. We anticipate receiving topline results in the first quarter of 2018 and, if positive, submitting an NDA in 2018. We designed our Phase 2/3 trial to support regulatory approval in the United States as well as to support regulatory filings in Europe and Japan. We also intend to explore the development of trigriluzole in adjacent

cerebellar disorders, including Friedreich's ataxia and sporadic ataxia, and potentially other neurological indications.

- Demonstrate bioequivalence and prepare for commercialization of our low-dose, oral disintegrating sublingual product candidate, BHV-0223, for ALS patients. We have completed Phase 1 testing of BHV-0223, our sublingually absorbed, oral disintegrating tablet, or ODT, formulation of riluzole, and intend to pursue regulatory approval of BHV-0223 for ALS in the United States under Section 505(b)(2) of the U.S. Federal Food, Drug and Cosmetic Act. We plan to launch a study to compare the bioequivalence of BHV-0223 to riluzole in 2017 and subsequently submit an NDA in 2018.
- Advance BHV-5000 into clinical trials to assess its potential to be the first approved treatment for patients suffering from breathing irregularities associated with Rett syndrome. We anticipate completing our commercial-grade formulation efforts for BHV-5000 in the third quarter of 2017. After a confirmatory Phase 2/3 trial to bridge pharmacokinetics with the prior formulation, we plan to initiate a Phase 2 trial in Rett syndrome in 2018. Once we establish proof-of-concept in Rett syndrome, we intend to explore the development of BHV-5000 in other neuropsychiatric indications.
- Maximize the therapeutic and commercial potential of our existing product candidates by exploring their use for multiple indications. Based on the broad mechanistic potential of our glutamate modulation platform, we believe that our product candidates may have utility in a wide array of conditions. We intend to explore the use of our product candidates in the development of treatments for multiple indications, beginning with orphan neurological indications, including SCA, Rett syndrome and ALS. If the results of our ongoing Phase 2/3 trial in SCA are positive, we intend to develop trigriluzole for the treatment of other ataxias as well. We also plan to potentially expand our pipeline into other therapeutic indications where glutamate plays a central role in the pathophysiology of disease, including anxiety and mood disorders.
- Actively manage our product portfolio and opportunistically enter into strategic collaborations. We have a pipeline of product candidates for both large market and rare disease opportunities. We believe that the broad mechanistic potential of our glutamate modulation platform could continue to significantly expand our pipeline. As we seek to commercialize any approved products, we intend to maintain a highly skilled, agile and cost-effective infrastructure focused on specialty drug development. We plan to retain our worldwide commercialization rights for some of our key product candidates while for other product candidates we will consider partnership opportunities to maximize returns. Leveraging our management team's deep large pharma relationships and experience will be a key component of this strategy as we continually assess U.S. and ex-U.S. partnership opportunities.

### **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 2010 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 migraine days per month for more than three months. Others have episodic migraine, which is characterized by experiencing less than 15 migraine days per month. People with episodic migraine may progress to chronic migraine over time. Migraine attacks can last a few hours or up to 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 therapy for 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 one of the more commonly prescribed triptans. 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.

The prevention of chronic and episodic 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, or Botox, and generate nearly 10 million prescriptions annually.

In patients with high frequency and chronic migraine, beta blockers, topiramate and sodium valproate are commonly used. These medications are often not well tolerated by patients because of adverse events 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 6-7 days at baseline, or reduced by 3.5 days from 15-16 days at baseline. Migraine is twice as prevalent in women as compared to men. In the affected female patient population, predominantly women of childbearing age, the association of these agents with poor pregnancy outcomes and fetal abnormalities can limit their use. Botox is only approved in patients with 15 or more migraine days per month. 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.

We believe BHV-3500 has the potential to address a significant unmet need as well as compete effectively with current and future migraine prevention therapies. BHV-3500 may afford multiple routes of delivery including daily oral administration for the prevention of chronic 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.

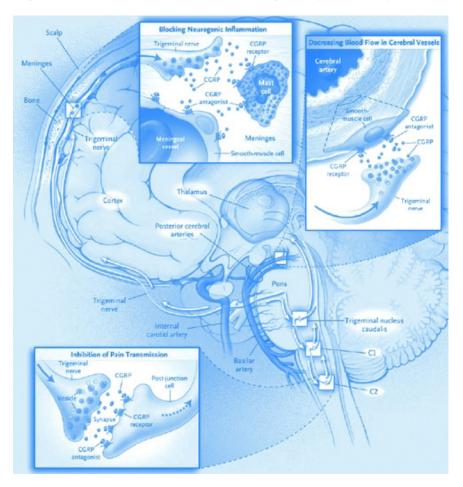
### CGRP's Role in Migraine

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 normalize CGRP levels. Additionally, multiple clinical studies show that small molecule CGRP receptor antagonists, which inhibit the binding of endogenous CGRP to CGRP receptors, are effective in aborting migraine attacks.

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

- Blocking Neurogenic Inflammation: Binding of CGRP receptor antagonists to CGRP receptors located on mast cells would inhibit 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 would 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 would suppress the transmission of pain by inhibiting the central relay of 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.



N Engl J Med, Paul L. Durham, "CGRP-Receptor Antagonists-A Fresh Approach to Migraine Therapy," March 11, 2004. Copyright © Massachusetts Medical Society.

### Our Lead Product Candidate: Rimegepant, an Oral CGRP Receptor Antagonist for Acute Treatment of Migraine

We are developing rimegepant as an orally available, selective and potent small molecule CGRP receptor antagonist for the acute treatment of migraine. We believe that rimegepant has the potential to be the best-in-class CGRP receptor antagonist for the treatment of migraine with the ability to address important unmet needs, such as durable efficacy across all four traditional migraine symptoms and reduced incidence of headache recurrence, without contraindications or warnings in patients with cardiovascular disease or cardiovascular risk factors such as hypertension.

Rimegepant dosed at 75 mg was observed to have statistically significant, durable improvement as compared to placebo in a Phase 2b, double-blind, randomized, placebo-controlled, dose-ranging clinical trial completed by BMS. In this trial, 812 patients suffering from migraine attacks received either placebo, sumatriptan 100 mg (a currently approved triptan medication for migraine) or rimegepant dosed at 10, 25, 75, 150, 300 or 600 mg. The Phase 2b data showed statistically significant effects of rimegepant starting at the 75 mg dose compared to placebo, meaning that at this dose level, statistically significant results were observed on all four key migraine symptoms—pain, nausea, photophobia and phonophobia. Higher doses of rimegepant, while also showing improvement compared to placebo, did not appear to convey any meaningful additional benefit above the 75 mg dose. The observed improvement profile is consistent with the published literature showing a lack of a progressive dose-response curve for acute anti-migraine drugs. To our knowledge and based on publicly available information, rimegepant is the only small molecule CGRP receptor antagonist currently in development that has achieved statistically significant improvement on all four of the traditional endpoints within a single study, which suggests a broad efficacy profile important both to patients and physicians. Rimegepant also was observed to have evidence of durable improvement as demonstrated by statistically significant effects on two-to-24 hour and two-to-24 hour pain freedom and two-to-24 hours after dosing and, with respect to pain freedom, through 48 hours after dosing. This durable improvement is significant because other common migraine medications, such as triptans, have been associated with headache recurrence.

The Phase 2b trial successfully completed its aim of identifying a Phase 3 dose. Based on these observations, we are advancing the 75 mg dose of rimegepant in our Phase 3 clinical trials. In the second half of 2017, we plan to commence two Phase 3 clinical trials of rimegepant for the acute treatment of migraine, with topline results expected in the first quarter of 2018.

### 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, NSAIDs, opioids and combination medications. The current standard of care for the acute treatment of migraine is prescription of triptans, which are serotonin 5-HT1B/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, only about 30% of patients from clinical trials are pain free at two hours after taking triptans. 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 recent 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, less stringent draft guidance indicating that pivotal migraine trials could use co-primary endpoints of freedom from pain and most bothersome symptom to support approval. We believe rimegepant may be superior to other acute treatments for migraine currently approved and in development because, based on our Phase 2b clinical trial data, rimegepant was observed to result in statistically significant improvement in all four endpoints of pain, nausea, photophobia and phonophobia at the 75 mg dose, compared to placebo, with a favorable safety profile.

The table below compares key features of rimegepant to two other product candidates targeting migraine that are currently in development and that we anticipate could receive marketing approval as

early as 2019-2020, and to CGRP antibodies, which represent another class of migraine-targeting product candidates in development.

Compound	Rimegepant	Ubrogepant	Lasmiditan	CGRP Antibodies
Mechanism of Action	CGRP receptor antagonist	CGRP receptor antagonist	5-HT1F receptor agonist	CGRP antibodies
Stage of Development	Phase 3 ready	Phase 3	Phase 3	Phase 3 and earlie
Effectiveness in Acute Treatment of Migraine	<ul> <li>Comprehensive treatment effect: pain, nausea, photophobia and phonophobia at 2 hours post-dose in a Phase 2b trial</li> <li>Durable treatment effect: 2 - 24 and 2 - 48 hour sustained pain freedom</li> </ul>	<ul> <li>Improvement in pain, photophobia and phonophobia</li> <li>Comprehensive treatment effect: did not show improvement on nausea or pain relief at 2 hours in Phase 2</li> <li>Durable treatment effect: did not show 2 - 48 hour sustained pain freedom at 1 - 50 mg in Phase 2 (present at 100 mg)</li> </ul>	<ul> <li>✓ Improvement shown in pain and most bothersome</li> <li>× Durable treatment effect: Phase 2 – Headache recurrence at 24 hours not different from placebo Phase 2/3 – No data showing 2 - 24 or 2 - 48 hour sustained pain freedom or sustained pain relief</li> </ul>	<ul> <li>Preventative use only</li> <li>Durable treatment effect: vast majorit of patients show residual acute migraines</li> </ul>
Safety / Tolerability	✓ Well tolerated	✓ Well tolerated	<ul> <li>Phase 2 – Higher rates of severe AEs and treatment- emergent AEs compared to placebo (dizziness, fatigue, vertigo, paresthesias, somnolence and sensation of heaviness)</li> <li>Phase 3 – Higher rates of treatment-emergent AEs compared to placebo (dizziness, paresthesia, somnolence, nausea, fatigue, lethargy and vertigo)</li> </ul>	<ul> <li>✓ Well tolerated</li> <li>× Cumbersome rout of administration (IV, SC)</li> </ul>
Benefits / Considerations of Mechanism	<ul> <li>Novel alternative for patients who are triptan intolerant or unresponsive</li> <li>No reason to expect headache recurrence phenomena</li> </ul>	<ul> <li>Novel alternative for patients who are triptan intolerant or unresponsive</li> <li>No reason to expect headache recurrence phenomena</li> </ul>	<ul> <li>Mechanism represents an advance on triptans</li> <li>Uncertainty regarding triptans — e.g., rebound</li> <li>Uncertain appeal in triptan non-responders</li> </ul>	<ul> <li>Monoclonal antibody directed against circulating CGRP or CGRP receptors</li> </ul>

Based on the results from the Phase 2b trial and earlier-stage development, we believe rimegepant offers the following clinical and product benefits for the acute treatment of migraine:

- **Oral Availability.** To our knowledge, rimegepant is one of only two small molecule CGRP receptor antagonists that is currently in late-stage clinical development and that offers patients convenient oral administration.
- **Comprehensive Treatment Effect.** In the Phase 2b trial, the 75 mg dose of rimegepant showed statistically significant improvement as compared to placebo across all four key migraine symptoms (pain, nausea, photophobia and phonophobia), while the other small molecule CGRP receptor

antagonists currently in development have failed to show statistically significant improvement on nausea, and also failed to show significant improvement on pain relief.

- **Durable Improvement.** In the Phase 2b trial, the improvement of the 75 mg dose of rimegepant on pain freedom was statistically significant at two-to-24 hours and two-to-48 hours after dosing, and on pain relief was statistically significant at two and 24 hours after dosing, in each as compared to placebo, showing durability of treatment effect.
- **Favorable Safety Profile.** In the Phase 2b trial, rimegepant was generally well tolerated with low rates of adverse events, or AEs, no discontinuations for AEs, no treatment-related serious adverse events and no deaths. Adverse events in the 75 mg treatment group were comparable to the placebo group, and most adverse events across all treatment groups were mild to moderate in intensity and dose-dependent. Rimegepant does not cross the blood brain barrier, so there is low potential for centrally mediated adverse effects. In addition, the preclinical and clinical evidence suggests that CGRP receptor antagonists, such as rimegepant, have an absence of vasoconstrictor activity and lack 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.
- **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. To date, the majority of clinical and preclinical development with rimegepant has been conducted by BMS. 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.

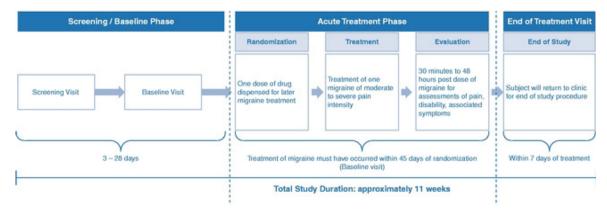
#### Phase 2b Clinical Trial Design and Results

Rimegepant is being developed for oral administration and was observed to have evidence of comprehensive and durable treatment effect in a large Phase 2b clinical trial conducted by BMS. This Phase 2b clinical trial, the results of which were published in 2014, was a double-blind, randomized, placebo-controlled, dose-ranging trial of rimegepant for the acute treatment of migraine. The primary

objective was to evaluate the efficacy of rimegepant compared with placebo in the acute treatment of migraine as measured by pain freedom (head pain intensity level reported as "no pain") at two hours post-dosing using a four point rating scale (no pain, mild pain, moderate pain, severe pain) while identifying an optimal dose to support the Phase 3 clinical trials. Subjects were randomized to receive placebo, a 100 mg dose of sumatriptan or one of six doses of rimegepant (10 mg, 25 mg, 75 mg, 150 mg, 300 mg, or 600 mg). Randomization made use of an adaptive design, whereby one quarter of subjects were assigned placebo and one-eighth were assigned sumatriptan; the remainder were assigned to one of six rimegepant groups based on a Bayesian analysis of the observed response rates. Subjects were instructed to treat one migraine of moderate to severe pain intensity and return to the clinic within seven days.

A total of 885 subjects were randomized and 812 completed the study (the remaining subjects did not experience a migraine during the treatment phase of the trial). Key entry criteria included: age 18 to 65 inclusive with at least a one-year history of migraine beginning prior to 50 years of age; migraine attacks lasting four to 72 hours if left untreated; not more than eight attacks per month of moderate or greater severity over the prior three months; and less than 15 total headache days per month (migraine plus non-migraine) in each of the three preceding months.

Patients were given an electronic diary to record improvements and returned to the study site within seven days of study treatment for review of the data. Patients who experienced relief of headache pain to a mild intensity or pain-free intensity level at two hours postdosing were considered to be responders. The patients who did not experience such relief at the end of two hours were permitted to use an approved rescue medication. Use of rescue medication within 48 hours was also recorded. Whatever the case, the patient was required to continue to complete his or her electronic diary for up to 48 hours after dosing. Secondary efficacy variables included total migraine freedom: a composite endpoint consisting of freedom from headache pain coupled with no symptoms of photophobia, phonophobia or nausea, at two hours post-dosing, and sustained pain freedom from two to 24 hours. Exploratory measures included pain relief at two hours post-dosing, sustained pain freedom from two to 48 hours post-dosing. Safety variables included AEs, serious adverse events, or SAEs, clinical laboratory evaluations, vital sign measurements, physical examinations, and electrocardiograms, or ECGs. The following graphic illustrates the study design of the Phase 2b clinical trial:



With regard to the primary study outcome, the percentage of patients who were pain free at two hours after dosing is depicted in the figure below. The rimegepant 75 mg, 150 mg, and 300 mg dose groups each were significantly superior to placebo ( $p \le 0.01$ ). Among the rimegepant dose groups, the percentage of subjects who were pain free at two hours after dosing was 31.4% (27/86) in the 75 mg group; 32.9% (28/85) in the 150 mg group; and 29.7% (33/111) in the 300 mg group, compared to 15.2% of patients in the placebo group. Statistical separation from placebo was not seen with the 600 mg group (24.4%, 20/82) as compared to the lower doses.

50 \*\*p<0.01 \*\* 35.0 32.9 31.4 \*\* Proportion of Patients (%) 29.7 40 24.4 19.7 19.7 30 15.2 20 10 0 Placebo Sumatriptan 10 mg 25 mg 75 mg 150 mg 300 mg 600 mg 100 mg Rimegepant 71 82 n = 203 100 61 86 85 111 p value = < 0.0001 0.3925 0.4021 < 0.0018 0.0005 < 0.0024 0.0737

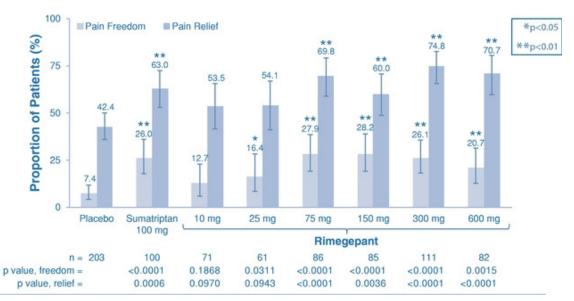
# Pain Freedom 2 hours Post-Dosing (+/- 95% Confidence)

The table below shows the percentage of patients in the placebo, sumatriptan, and each rimegepant dose groups who experienced pain freedom and pain relief in the trial, and the corresponding p-values. P-value is a conventional statistical method for measuring the statistical significance of clinical results. A p-value of 0.05 represents statistical significance, meaning that there is only a 5% likelihood that the observed results occurred by chance. The table shows that rimegepant 75 mg showed statistically significant improvements compared to placebo on sustained pain freedom from two-to-24 hours and two-to-48 hours post-dose, on pain relief two hours post-dose and on sustained pain relief from two-to-24 hours post-dose (all with a 0.1% likelihood that the observed results were merely due to chance).

	Placebo	Sumatriptan	Rimegepant					
Patients, %	n=203	100 mg n=100	10 mg n=71	25 mg n=61	75 mg n=86	150 mg n=85	300 mg n=111	600 mg n=82
Sustained Pain Freedom (2-24 Hours Post-Dose)	7.4	26.0	12.7	16.4	27.9	28.2	26.1	20.7
p Value		<0.001	0.19	0.031	<0.001	<0.001	<0.001	0.002
Sustained Pain Freedom (2-48 Hours Post-Dose)	7.4	26.0	11.3	14.8	27.9	28.2	26.1	20.7
<i>p</i> Value		<0.001	0.33	0.074	<0.001	<0.001	<0.001	0.002
Pain Relief (2 Hours Post-Dose)	51.2	72.0	59.2	60.7	72.1	61.2	75.5	78.0
p Value		<0.001	0.21	0.16	<0.001	0.058	<0.001	<0.001
Sustained Pain Relief (2-24 Hours Post-Dose)	42.4	63.0	53.5	54.1	69.8	60.0	74.8	70.7
p Value		<0.001	0.097	0.094	<0.001	0.004	<0.001	<0.001

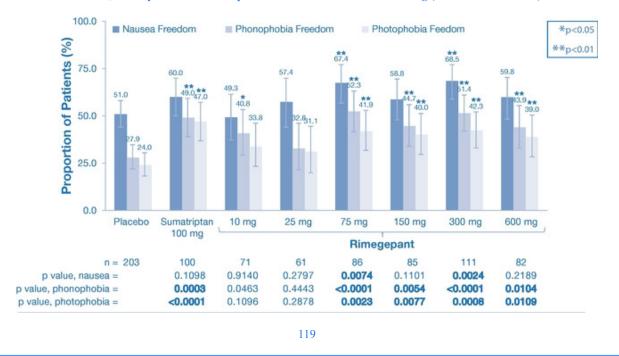
Bold: Statistical significance over placebo treatment.

The figure below shows the percentage of patients who reported sustained pain freedom and sustained pain relief at two-to-24 hours after dosing among the placebo dose group, the sumatriptan dose group, and each dose group of rimegepant. Rimegepant was statistically superior to placebo on pain freedom and pain relief at two-to-24 hours across all dose groups 75 mg and above.



Sustained Pain Freedom and Pain Relief 2-24 Hours Post-Dosing (+/-95% Confidence)

The figure below shows the Phase 2 trial results for the three other traditional co-primary endpoints previously required by the FDA—freedom from nausea, phonophobia and photophobia, showing the proportion of patients with alleviation of these symptoms at two hours after dosing in the placebo dose group, the sumatriptan dose group, and in each of the rimegepant dose groups. Rimegepant 75 mg was statistically superior to placebo on nausea, photophobia and phonophobia freedom at two hours after dosing.



Nausea, Phonophobia and Photophobia Freedom 2 Hours Post-Dosing (+/- 95% Confidence)

With regard to safety and tolerability in the Phase 2 clinical trial, the overall incidence of AEs was comparable across the placebo and rimegepant treatment groups. The most commonly seen AE in the rimegepant dosing groups was nausea, which appeared to exhibit a dose dependent trend at the higher doses: 1.4% in the 10 mg dose group; 0% in the 25 mg dose group; 3% in each of the 75 mg and 150 mg dose groups; 4% in the 300 mg dose group; and 8% in the 600 mg dose group. Importantly, although the patient numbers were small, the reported events of chest discomfort, chest pain, muscle tightness, and jaw pain were only observed in the sumatriptan-treated patients, with no rimegepant treated patients reporting chest pain-related symptoms. Most of the adverse events reported were mild to moderate in intensity. Two serious adverse events were reported (post-lumbar puncture headache and pneumonia), but neither was deemed by the trial investigators to be treatment-related. No deaths were reported, and no patients discontinued because of AEs. There were no clinically important ECG findings, vital sign abnormalities, or physical examination findings after administration of rimegepant.

The table below shows the number and percentage of patients reporting a commonly occurring AE within 48 hours post-dosing. Rimegepant was generally well tolerated with no events of chest discomfort and low rate of AEs across dose groups.

Placebo	Sumatriptan	Rimegepant					
n=209		10 mg n=72	25 mg n=62	75 mg n=86	150 mg n=86	300 mg n=112	600 mg n=84
5 (2)	2 (2)	1 (1)	0	3 (3)	3 (3)	5 (4)	7 (8)
2 (1)	1 (1)	2 (3)	1 (2)	1 (1)	2 (2)	0	3 (4)
5 (2)	1 (1)	0	2 (3)	2 (2)	0	0	2 (2)
0	0	4 (6)	0	0	0	1 (1)	0
2 (1)	2 (2)	0	0	0	0	0	0
0	0	2 (3)	0	0	0	0	0
0	2 (2)	0	0	0	0	0	0
0	0	2 (3)	0	0	0	0	0
	n=209 5 (2) 2 (1) 5 (2) 0 2 (1) 2 (1) 0 0	100 mg n=209         100 mg n=100           5 (2)         2 (2)           2 (1)         1 (1)           5 (2)         1 (1)           5 (2)         1 (1)           0         0           2 (1)         2 (2)           0         0           2 (1)         2 (2)           0         0           0         0           0         0           0         0	$\begin{array}{ c c c c c c c c }\hline & 100 \text{ mg} & 10 \text{ mg} \\ n=209 & n=100 & n=72 \\ \hline 5 & (2) & 2 & (2) & 1 & (1) \\ \hline 2 & (1) & 1 & (1) & 2 & (3) \\ \hline 5 & (2) & 1 & (1) & 0 \\ \hline 5 & (2) & 1 & (1) & 0 \\ \hline 0 & 0 & 4 & (6) \\ \hline 2 & (1) & 2 & (2) & 0 \\ \hline 0 & 0 & 2 & (3) \\ \hline 0 & 2 & (2) & 0 \\ \hline \end{array}$	$\begin{array}{ c c c c c c c c c c c c c c c c c c c$	$\begin{array}{ c c c c c c c c c c c c c c c c c c c$	$\begin{array}{ c c c c c c c c c c c c c c c c c c c$	$\begin{array}{ c c c c c c c c c c c c c c c c c c c$

Adverse events occurring in >2% of patients in any treatment group; ordered by frequency in the Rimegepant 600 mg group. n: number (%) of patients who took at least one tablet of the study medication.

Treatment-emergent AEs that occurred within two hours post-dosing were reported most often in the sumatriptan group (10.0%), followed by the 600 mg (8.3%), 300 mg (8.0%), 150 mg (7.0%), 10 mg (6.9%), 25 mg (4.8%), and the 75 mg (4.7%) dose groups, and the placebo group (2.9%). In the rimegepant dose groups, the most common adverse events reported within two hours post-dosing were primarily low rates of dizziness and somnolence, and gastrointestinal disorders, primarily nausea and vomiting.

The liver has been a target of interest in certain small molecule CGRP receptor antagonists, as indications of liver toxicity have been associated with frequent use. In the Phase 2b trial, one patient in the rimegepant 75 mg dose group and one patient in the placebo group had a report of an asymptomatic and mild increase in certain hepatic enzymes, which are types of liver enzyme measured in a liver function test to detect damage and inflammation to the liver. The subject in the rimegepant 75 mg dose group had peak alanine transaminase, or ALT, and aspartate transaminase, or AST, elevations that were less than 1.22 times the upper limit of normal (ULN) and reported as an AE, while the placebo subject had a total bilirubin level that was greater than 2xULN. No subjects in the Phase 2b trial had AST or ALT elevation that exceeded 3xULN, a level that is considered to be a potentially meaningful indicator of a drug's potential to cause severe drug-induced liver injury, or DILI, based on FDA guidance.

In conclusion, in the Phase 2b clinical trial, rimegepant was observed to be superior to placebo in the acute treatment of migraine and the trial identified the lowest dose that is fully effective in patients. More specifically, the selection of 75 mg rimegepant as the dose for advancement in Phase 3 trials was based on observed improvement as compared to placebo on the key primary outcome measure, pain freedom at two hours (31.4% vs 15.2% placebo; p = 0.0018) and key secondary and exploratory outcome measures: total

migraine freedom at two hours (27.9% vs 11.8%; p = 0.0008), sustained pain freedom two to 24 hours (27.9% vs 7.4%, p < 0.0001), freedom from photophobia at two hours (41.9% vs 24.0%, p = 0.0023), freedom from photophobia at two hours (52.3% vs 27.9%, p < 0.0001), freedom from nausea at two hours (67.4% vs 51.0%, p = 0.0074), pain relief at two hours (72.1% vs 51.2%, p = 0.0007), and sustained pain relief from two-to-24 hours (69.8% vs 42.4%, p < 0.0001). Notably, rimegepant is the only small molecule and orally available CGRP receptor antagonist that has shown statistically significant improvement on the key migraine symptoms of pain, nausea, photophobia and phonophobia in a single trial.

# Phase 3 Clinical Trial Development Plan

Based on the results of the Phase 2 clinical trial, we have elected to advance the 75 mg dose of rimegepant in our proposed 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 for approval based on an effect on headache pain freedom and 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 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 had an end of Phase 2 meeting with the FDA in March 2017 and we plan on conducting two Phase 3 registrational trials commencing in 2017. Both trials will conform to the FDA guidance for approval in acute treatment of migraine. The trials will be doubleblinded, randomized, and placebo controlled. The trials will recruit 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 is to enroll patients who represent the spectrum of real-world migraineurs, 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 are also enrolling patients who have cardiovascular risk factors and/or vascular disease. The primary objective of the trials will be 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) will be assessed as secondary endpoints.

In designing the Phase 3 trials, care was taken to minimize any changes in study populations compared to the already completed Phase 2 trial with rimegepant with no major changes in inclusion and exclusion criteria between the completed and planned trials. The main differences in trial design between the previous Phase 2 trials and our planned Phase 3 clinical trials include:

1. Change in the primary outcome measure and statistical analysis plan to conform to recent FDA guidance. The Phase 2b trial identified pain freedom at two hours as the primary outcome measure and included various secondary and exploratory outcome measures to assess the associated symptoms of nausea, photophobia and phonophobia. The Phase 3 trials utilize pain freedom and freedom from MBS at two hours after dosing as co-primary endpoints. In addition, to conform to recent FDA guidance, we intend to analyze the data collected in our Phase 3 trials on an intent-to-treat basis, rather than on a modified per-protocol basis, which was the basis on which the data was analyzed in the Phase 2 trial;

- 2. *Number of treatment arms*. The Phase 2b trial included six different dose groups of rimegepant, sumatriptan and placebo arms. The Phase 3 trials will only include 75 mg rimegepant versus placebo, since 75 mg rimegepant was identified as the lowest dose in the Phase 2b trial at which improvements were observed in the four key migraine symptoms; and
- 3. *Increase in sample size*. The sample size calculations for each treatment arm in the Phase 3 trial will be approximately 425 patients, which were determined based upon the observed effect size from the Phase 2b trial.

This change in the hierarchy of outcome measures, sample size and number of treatment arms reflect somewhat standard changes in clinical trial design to increase technical and regulatory chances of success in the registrational program. We are also developing a commercial-grade formulation of rimegepant that we plan to use in our Phase 3 clinical trials. We intend to submit our trial protocols to the FDA prior to the commencement of our Phase 3 trials. The FDA may have additional feedback on our trial design.

We are also planning a long-term safety study to meet FDA requirements for approval. This study will be a 12-month, long-term, open label safety study conducted in patients with migraine. Two thousand patients will be treated in this study. A subset of patients (approximately 600) will have 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 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. Study visits for all patients will be 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 will administer liver function testing at two weeks post-dose and will follow patients with any abnormal liver function tests until clinical resolution. We intend to initiate this study in 2017.

### Previous Clinical Trials with Rimegepant

To date, six clinical trials have been 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 safe and 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.

Approximately 687 subjects have been dosed with rimegepant to date. In Phase 1 and 2b trials, approximately 600 subjects have received single doses of rimegepant, ranging from 25 mg to 1500 mg; and approximately 87 subjects have received multiple doses of rimegepant, ranging from 75 mg to 600 mg daily for up to 14 days. 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 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.

As of December 31, 2016, only two SAEs have been reported in the rimegepant program, neither considered related to study drug: one subject had an SAE of severe post-lumbar puncture headache seven

days after exposure to a single dose of rimegepant that was considered unrelated to study treatment, and one subject had an SAE of moderate pneumonia with onset five days after exposure to a single dose of rimegepant that was considered unrelated to treatment. In addition, one subject who received placebo experienced an SAE (appendicitis).

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 are ongoing to assess effects at therapeutic doses of rimegepant.

# 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 CNS systems. 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. 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, the primary target organ effect was minimal to moderate macrophage accumulation (histiocytosis) in mandibular and mesenteric lymph nodes in males at 100 mg/kg/day (at least 66× (for rats) and 123× (for monkeys) the anticipated maximum human AUC at a 75 mg/day clinical dose) in the 3-month study that was considered to be a marginal exacerbation of a common spontaneous change in this species. 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. 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 drug induced liver injury, or DILI, are reported as SAEs. There have been no reported cases of DILI with rimegepant administration to date. Other symptoms or target organs from nonclinical studies that will continue to be followed include skeletal muscle effects, emesis, skin rash and hematology measures.

#### Our Product Candidate BHV-3500, a CGRP Receptor Antagonist for Migraine Prevention

BHV-3500 is the second compound from our CGRP receptor antagonist platform. We are developing BHV-3500 for the prevention of chronic and episodic migraine, 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, or mAbs, that are currently in development which have a more cumbersome route of administration to patients in the form of intravenous or subcutaneous use.
- **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 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 chronic and episodic migraine, 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/backup intranasal formulation for rapid onset of action in the acute treatment of migraine.

#### Clinical Development Plans

We are planning to commence a toxicology development program in the first half of 2017 to support the submission of an IND for BHV-3500. This preclinical program will include intranasal and subcutaneous dose toxicity studies. If these studies support the submission of an IND, we would then plan to commence a Phase 1 clinical trial in the second half of 2017 to assess safety, tolerability and pharmacokinetics of BHV-3500 in healthy volunteers.

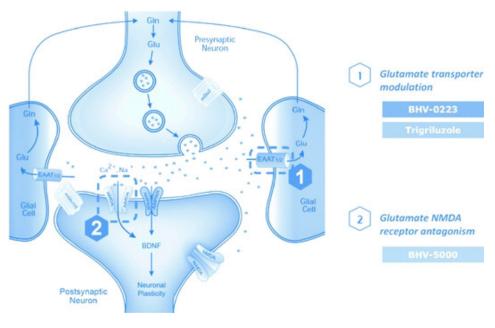
#### **Our Glutamate Platform**

We are developing three product candidates, trigriluzole, 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 (trigriluzole and BHV-0223) and glutamate 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, or 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 presynaptic 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 trigriluzole increase the activity of the EAATs to increase the clearance of glutamate and decrease glutamate release from the pre-synaptic neuron. Trigriluzole 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, or 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 trigriluzole.

We are currently developing trigriluzole as the potential first FDA-approved drug treatment option for patients suffering from ataxia, initially focusing on SCA. 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. If the results of our ongoing Phase 2/3 trial in SCA are positive, we will seek to expand to adjacent ataxias that have similar pathophysiology and represent significant potential for market expansion. According to Orphanet, in the United States, approximately 6,400 patients suffer from Friedreich's ataxia, 3,200 to 28,000 patients have sporadic ataxia, and 84,000 have acquired ataxias. There are currently no FDA-approved medications for the treatment of SCA or any other cerebellar ataxias. Our regulatory approval strategy for trigriluzole for ataxias will focus on obtaining additional orphan drug designations and exclusivity whenever they are available.



In addition, preclinical and small-scale pilot studies are underway to explore trigriluzole's use in the treatment of a pipeline of other indications such as essential tremor, neurodegenerative disorders, including ALS and Alzheimer's disease, and neuropsychiatric disorders, including anxiety and depression. We are also developing analogs of trigriluzole and other-related prodrugs for potential use in these separate indications.

We are currently developing BHV-0223 for the treatment of ALS. 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 only drug approved by the FDA for the treatment of ALS, riluzole is the established standard of care. However, while the market is highly genericized, there have not been further clinical improvements or advances in ALS drug therapeutics since the FDA's approval of riluzole in 1995. In addition, the use of riluzole is limited by a number of non-desirable attributes. We believe that BHV-0223, if approved, could gain meaningful market share, based on its favorable formulation attributes and a pricing model similar to that of branded Rilutek.

# **Our Product Candidate Trigriluzole for Ataxias**

Trigriluzole is an NCE and tripeptide prodrug of the active metabolite, riluzole. Based on its mechanism of action, preclinical data and clinical studies, trigriluzole has potential for therapeutic benefit in a range of neurological and neuropsychiatric illnesses. Initial development will focus on its use in SCA, an orphan neurological indication that currently has no approved therapies and for which the active metabolite has demonstrated preliminary efficacy in two prior randomized controlled trials conducted by third parties. We acquired trigriluzole from ALS Biopharma, LLC, or ALS Biopharma, and Fox Chase Chemical Diversity Center, Inc., or 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. Trigriluzole 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, trigriluzole 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. Trigriluzole 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 selection pathway that was pursued with trigriluzole 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 trigriluzole 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 via selection of linker moiety. 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 trigriluzole. Trigriluzole 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 barrier to entry from competitors. Trigriluzole 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 trigriluzole's active metabolite, riluzole, in two randomized controlled trials in patients with SCA and other ataxias conducted by third parties (Ristori 2010; Romano 2015). If the results of our ongoing Phase 2/3 trial in SCA are positive, we intend to conduct registrational trials to support approval in adjacent ataxia indications, such as Friedreich's ataxia and sporadic ataxia. In addition, based on preclinical studies and early-stage clinical trial results of riluzole, the active metabolite of trigriluzole, we believe trigriluzole or an optimized alternative prodrug from our pipeline may have potential therapeutic benefit in broader neurological conditions, such as essential tremor, Alzheimer's disease, obsessive compulsive disorder, bipolar disorder and generalized anxiety disorder, and in other diseases such as metastatic melanoma.

# 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.

# The Potential Benefits of Trigriluzole Compared to Riluzole

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

- **Improved Bioavailability**—Trigriluzole 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**—Trigriluzole 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 trigriluzole. 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 trigriluzole will reduce the potential for adverse liver effects.

- **Optimized Dosing Regimen and Compliance**—Trigriluzole 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**—Trigriluzole is highly soluble and does not exhibit the profound oral numbness associated with riluzole tablets. As such, we believe trigriluzole has the potential to be developed in multiple formulations including intranasal, subcutaneous, intravenous, sublingual and other forms.

### Our Clinical Program for Trigriluzole in Spinocerebellar Ataxia

Based on the results of our Phase 1 trial with trigriluzole and two third-party academic trials that have shown preliminary efficacy of riluzole in cerebellar ataxias, we are advancing trigriluzole into a Phase 2/3 clinical trial for SCA. We believe this trial, if successful, may be sufficient to support our application for regulatory approval of trigriluzole.

A summary of these third-party publications regarding the active metabolite of trigriluzole, riluzole, is provided below. 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, placebocontrolled 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 trigriluzole, may confer acute therapeutic effects after eight weeks of dosing in diverse forms of cerebellar ataxia.

Riluzole Group	Placebo Group	P-value	
n=19	n=19		
-7.05 (4.96%)	0.16 (2.65%)	<0.001	
-2.11 (2.75%)	0.68 (1.94%)	<0.001	
-4.11 (2.96%)	0.37 (2.0%)	<0.001	
-0.74 (0.81%)	0.05 (0.4%)	<0.001	
-0.16 (0.9%)	0.11 (0.66%)	0.838	
	n=19 -7.05 (4.96%) -2.11 (2.75%) -4.11 (2.96%) -0.74 (0.81%)	n=19         n=19           -7.05 (4.96%)         0.16 (2.65%)           -2.11 (2.75%)         0.68 (1.94%)           -4.11 (2.96%)         0.37 (2.0%)           -0.74 (0.81%)         0.05 (0.4%)	

Bold: Statistical significance 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 trigriluzole, in the treatment of cerebellar ataxia.

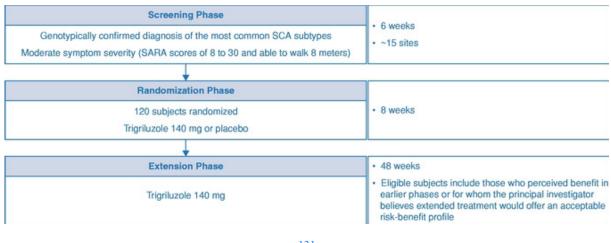
		Riluzole Group	Placebo Group	_ OR (95%) or Mean	P-value	
Patients, n (%)		n=28	n=27	Difference (95% CI)		
Primary Endpoint: Proportion	Yes	14 (50%)	3 (11%)	8.00 (1.95 to 32.83)	0.002	
of patients with improved SARA score at month 12	No	14 (50%)	24 (50%)			
Proportion of patients with improved SARA score at	Yes	14 (50%)	7 (26%)	2.86 (0.92 to 8.89)	0.066	
month 3	No	14 (50%)	20 (74%)			
Changes in SARA score from	Month 3	-1.00 (1.75)	0.50 (2.28)	-1.50 (-2.59 to 0.40)	0.008	
baseline	Month 12	-1.02 (2.15)	1.67 (2.63)	-2.68 (-3.98 to 1.39)	0.001	

Bold: Statistical significance over placebo treatment.

# Development and Regulatory Pathway

Our clinical program for trigriluzole 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 trigriluzole also qualifies as an NCE and thereby is eligible for conventional regulatory data exclusivities. In December 2016, we began enrollment in a Phase 2/3 clinical trial of trigriluzole in adult subjects with SCA.

The Phase 2/3 trial is a randomized, double-blind, placebo-controlled trial being conducted at approximately 15 sites in the United States, followed by an open-label extension phase. Approximately 120 subjects will be randomized to receive a once-daily dose of either placebo or 140 mg trigriluzole. Patients will be stratified by diagnosis (genotype) and baseline severity (as measured by the patient's gait SARA score of  $\leq 4$  and >4). The randomization phase will last eight weeks. 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 will be patient time to perform an eight-meter walk test. Exploratory outcome measures will 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 will 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). In addition, subjects completing the eight-week treatment phase are eligible to participate in a 48-week open-label extension phase. We enrolled the first patient on December 15, 2016. Enrollment is expected to conclude in 2018, with topline results available in the first quarter of 2018. 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. The FDA has stated its concern that our use of the SARA scale, as currently constructed, as a primary endpoint is not appropriate in this trial. We plan to continue to interact with the FDA to discuss their concerns with the SARA and will consider incorporating any feedback in our analysis of the clinical trial data that we collect and measure with the SARA.



The following chart shows a summary of the trial design for our Phase 2/3 trial of trigriluzole:

### Previous Clinical Trials with Trigriluzole

In July 2016, we began a Phase 1 randomized, double-blind, placebo-controlled study to evaluate the safety, tolerability and pharmacokinetics of single and multiple ascending doses of trigriluzole in normal healthy volunteers. In this study, the initial safety and tolerability of trigriluzole 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 trigriluzole 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 trigriluzole, 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 trigriluzole 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 trigriluzole into Phase 2/3 clinical testing.

# Trigriluzole: Next Indications

Given the novel chemical properties of trigriluzole and its unique mechanism of action, we believe trigriluzole, 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. SCA was chosen as the lead indication based on a strong preclinical rationale, the results of the Ristori and Romano studies outlined above, and data from our own Phase 1 trial with trigriluzole. If we observe positive efficacy results in SCA, we believe this will provide further proof-of-concept that trigriluzole has therapeutic potential in other disorders of glutamate dysfunction and we plan to explore trigriluzole in adjacent cerebellar disorders, such as Friedreich's ataxia and sporadic ataxia, and other orphan indications. We also may select another optimized prodrug from our pipeline to develop for the treatment of broader applications.

A brief description of potential indications that we could pursue in the future with trigriluzole 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 the results of our Phase 2/3 trial in SCA are positive, we believe the trial will provide validation for the role of trigriluzole in a range of other ataxias. Additionally, preliminary data from the Ristori and Romano randomized controlled trials 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 intend to explore additional trials in other ataxia indications, such as Friedreich's ataxia and sporadic ataxia.

• <u>Friedreich's Ataxia</u>: 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.

• <u>Sporadic Ataxia</u>: 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

• <u>Essential Tremor</u>: Like SCA, the pathophysiology of essential tremor, or 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 trigriluzole in mouse genetic and toxicity models of ataxia have shown reductions in tremor. Supported by this data, a pilot study of trigriluzole in approximately 20 subjects with ET is planned to start in 2017 in coordination 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 trigriluzole, 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

• *Obsessive Compulsive Disorder:* Obsessive compulsive disorder, or 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, or 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. 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 trigriluzole or another optimized prodrug of riluzole from our pipeline into a Phase 2 proof-of-concept trial in OCD.

- Generalized Anxiety Disorder: Generalized anxiety disorder, or GAD, is a neuropsychiatric disorder characterized by chronic or excessive worry, restlessness, fatigue, difficulty concentrating, or insomnia to such a degree that it causes diminished social or occupational functioning. Somatic symptoms such as irritable bowel-like gastrointestinal complaints are common. According to the Anxiety and Depression Association of America, GAD affects 6.8 million adults, or 3.1% of the U.S. population. According to the National Institute of Mental Health, only 43.7% of these patients receiving treatment are receiving minimally adequate treatment, which equates to only 18.9% of those with the disorder. Current first-line treatments include SSRIs, serotonin and norepinephrine reuptake inhibitors (duloxetine and venlafaxine), benzodiazepines and combinations thereof. Nonetheless, approximately half of patients do not respond adequately to these therapies and many patients are not amenable to treatment with these agents (e.g., due to tolerability or predisposition to substance abuse). GAD has significant societal and economic impact. For example, it is the most common contributor to workplace disability. In addition, patients with GAD utilize high levels of medical services; in addition to visiting psychiatrists to directly manage symptoms of GAD, patients visit internists and specialty clinicians to evaluate somatic complaints that range from headaches to fatigue to gastrointestinal distress. Our rationale for potentially advancing trigriluzole into a Phase 2 trial in GAD in the future is based on treatment effect in preclinical models of anxiety as well as favorable open-label case studies of patients treated with riluzole. In one case study, eight of 15 patients demonstrated a remission with a median response time of 2.5 weeks after starting riluzole 50 mg twice daily.
- Social Anxiety Disorder: Social anxiety disorder, or 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 selective serotonin reuptake inhibitors. 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 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 trigriluzole 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.

### Neurodegenerative Disorders

• Symptomatic treatment in Alzheimer's Disease: Alzheimer's disease, or AD, 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 5.4 million Americans with AD, 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 trigriluzole protects from AD-related pathology and cognitive dysfunction. In Alzheimer's disease, reduced glutamate uptake transporters have been reported in postmortem brain tissue of individuals with AD 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 trigriluzole, or another optimized prodrug of riluzole from our pipeline, in subjects with mild-to-moderate AD. We are advancing development in this indication by pursuing funding mechanisms, such as federal and foundation grants, and collaborations with clinical trial consortiums, including the University of California, San Diego.

### Other Indications Being Pursued by our Collaborators

Our collaborators are exploring the potential applicability of trigriluzole 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. Additional proof-of-concept work with trigriluzole is needed in these other indications to establish the likelihood of success in these other disease indications.

#### **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, there have not been further clinical improvements or advances in ALS drug therapeutics. Several therapies are currently in clinical trials. Riluzole extends survival and/or time to tracheostomy. 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

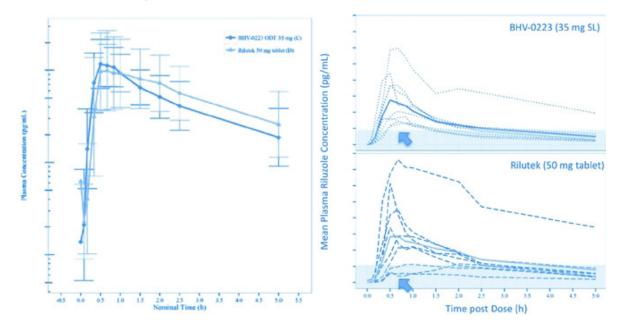
BHV-0223 is a formulation of riluzole designed to advance beyond the limitations of riluzole tablets for application in ALS. BHV-0223 is a sublingually absorbed and oral disintegrating tablet, or ODT, of riluzole, that makes use of proprietary Zydis ODT technology that we have exclusively licensed world-wide rights from Catalent U.K. Swindon Zydis Limited, or 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.

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 trial, we observed that BHV-0223 had less pharmacokinetic variability than 50 mg riluzole.
- **No Food Effect**—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.
- **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.

We recently completed a Phase 1 trial, in which we assessed the safety, tolerability and pharmacokinetics of BHV-0223. This study was a randomized, cross-over, controlled trial employing single and multiple doses of BHV-0223 (10 mg, 17.5 mg and 35 mg strengths delivered sublingually) as well as 50 mg Rilutek delivered orally. Sublingual dosing of 35 mg BHV-0223 delivered an exposure profile that was comparable to that achieved with oral delivery of 50 mg Rilutek tablets. BHV-0223, 35 mg dose, demonstrated a mean 15% greater extent of absorption compared to Rilutek on a dose-normalized basis, a comparable absolute peak concentration and increased early exposure consistent with sublingual absorption. In addition, pharmacokinetic variability appeared lower with sublingual BHV-0223 as compared to 50 mg Rilutek. For example, no subjects in the 35 mg BHV-0223 arm achieved low peak concentrations (i.e., <50 ng/mL) as compared to one-third of subjects who received 50 mg Rilutek. Based on pharmacokinetic modeling, 40 mg of BHV-0223 is the optimized dose strength for the purpose of fulfilling formal regulatory criteria for bioequivalence and is the dose strength that we have chosen to advance in future clinical trials.

In the Phase 1 trial, BHV-0223 was observed to be generally well tolerated following sublingual administration of doses ranging from 10 mg to 35 mg in healthy subjects. There were no clinically significant laboratory abnormalities or SAEs observed. The vast majority of AEs were mild in intensity, including oral hypoaesthesia. Overall, we believe these results demonstrate the potential of BHV-0223 in delivering riluzole via sublingual absorption in a well tolerated manner that can potentially offer patients with ALS a more favorable route of administration as compared to oral riluzole tablets.



The figures above show results from our Phase 1 trial comparing pharmacokinetics in healthy subjects dosed with sublingual BHV-0223 35 mg versus generic Rilutek 50 mg tablets, in a cross-over manner. In the left panel, mean concentrations of patients dosed with BHV-0223 35 mg were similar over time in the same subjects dosed with generic Rilutek 50 mg tablets. The right panel shows the mean concentrations of individual pharmacokinetic profiles superimposed. Notably, subjects dosed with generic Rilutek 50 mg tablets (lower portion of right hand panel) had greater pharmacokinetic variability and more than 30% of subjects showed low peak concentrations (i.e., <50 ng/mL) compared to the same subjects who were administered sublingual BHV-0223 35 mg (upper portion of right hand panel).

### Future Development and Regulatory Pathway

We intend to pursue regulatory approval of BHV-0223 for the treatment of patients with ALS in the United States under Section 505 (b)(2) of the U.S. Federal Food, Drug and Cosmetic Act. Our IND for BHV-0223 went into effect in August 2015. 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. We are planning to launch a pivotal bioequivalence study in 2017 comparing BHV-0223 to riluzole in healthy subjects. We plan to include a dosing arm to assess the impact of meals on drug absorption in order to potentially support dosing instructions that can avoid the need for the dietary restrictions that accompany Rilutek. If this trial is successful, we plan to subsequently submit an NDA to the FDA in 2018.

We also intend to conduct a clinical trial in healthy subjects to assess the effect of BHV-0223 on transaminase levels and other markers of liver function. We believe that these trials, if successful, may also be sufficient to demonstrate the clinical superiority of BHV-0223 to Rilutek.

#### **Glutamate NMDA Receptor Antagonism**

An *N*-methyl-D-aspartate, or 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. 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 the treatment of breathing irregularities associated with Rett syndrome, and we also intend to explore its application in other neurological or neuropsychiatric indications.

#### **Our Product Candidate BHV-5000 for 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.

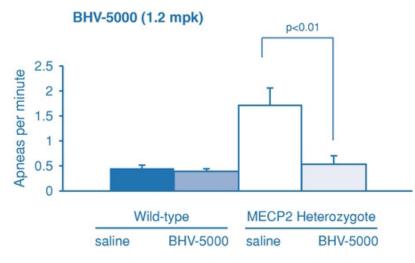
### Our Clinical Program for BHV-5000 in Rett Syndrome

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 adverse events 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.

# Future Clinical Development of BHV-5000

The 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 GLP toxicology, reproductive toxicology and carcinogenicity studies of lanicemine to potentially expedite the safety package for BHV-5000. We are in the process of developing a commercial formulation of BHV-5000 with acceptable shelf-life and stability at room temperature. Once this is completed, we intend to conduct a brief Phase 1 trial to characterize and confirm BHV-5000's pharmacokinetic attributes, which we plan to complete by the end of 2017. Subject to the satisfactory completion of the Phase 1 trial, we intend to enroll approximately 120 patients in the trial, and the patients will be randomly assigned to 24 weeks of treatment of either placebo or one of two dose levels of BHV-5000. The primary outcome measure will be reduction in respiratory abnormalities (number of apneic episodes), an endpoint that has been advanced with regulatory authorities and used by other sponsors. Reduction in apneic episodes is considered a meaningful benefit for patients and caregivers, both improving quality of life and potentially reducing secondary cardio-respiratory complications. In addition, we will observe impacts on other symptom domains as secondary outcome measures.

# BHV-5000: Next Indications

We believe that modulation of NMDA receptor activity has the potential for broad applicability across a number of CNS disorders. Our goal is to rapidly advance BHV-5000 into the treatment of breathing irregularities associated with Rett syndrome and then pursue development for other neurological or neuropsychiatric indications with high unmet medical needs. If the results of our proposed Phase 2/3 trial in Rett syndrome are positive, we believe this will serve as proof-of-concept for BHV-5000 across neuroscience indications, and we would then explore development of BHV-5000 in other conditions such as depression, neuropathic pain and other disorders involving NMDA receptor dysfunction.

### Major Depressive Disorder

Major depressive disorder, or 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.

# Kleo Pharmaceuticals, Inc.

In 2016, we invested \$3.0 million to acquire a minority interest in Kleo Pharmaceuticals, Inc., or Kleo, a privately held, preclinicalstage 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. Kleo has in-licensed technology from Yale University related to antibody recruiting molecules, or ARMs, and synthetic antibody mimics, or SyAMs. ARMs and SyAMs are bifunctional molecules composed of two active heads attached with a linker in-between that are designed to direct your immune system to fight specific disease-causing cells. We have also entered into a clinical development master services agreement with Kleo to assist Kleo with clinical development as its programs mature into clinical development.

As of December 31, 2016, we owned approximately 18.6% of Kleo's outstanding capital stock. In connection with our initial \$3.0 million investment in 2016, we agreed to invest an additional \$5.5 million in Kleo through December 2017. In March 2017, we satisfied our first purchase obligation by purchasing 1,375,000 shares of Kleo common stock for cash consideration of \$1.4 million. Separately, we also purchased 500,000 shares of Kleo common stock in March 2017 from one of Kleo's officers in exchange for aggregate consideration of \$249,750 in cash and 32,500 of our common shares.

#### 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 targeting acute treatment of migraine and migraine prevention, respectively, we face competition from companies that develop and/or sell the following types of migraine treatments:

#### **Triptans**

Clinicians use a number of pharmacologic agents for the acute treatment and/or prevention of migraine. Aside from the NSAID diclofenac, only one other class of acute migraine-specific medication,

serotonin 5-HT1B/1D receptor agonists, or triptans, has been developed and approved for the acute treatment of migraine over the past 15 years. The initial introduction of triptans represented a shift toward drugs more selectively targeting the suspected pathophysiology of migraine. We anticipate that the 5-HT1F receptor antagonist lasmiditan in development by CoLucid Pharmaceuticals, Inc. (which agreed to be acquired by Eli Lilly and Company in January 2017) could be approved as early as 2019. Lasmiditan does not directly target the CGRP receptor, but we expect that it would be approved prior to rimegepant. Lasmiditan was designed to act through non-vasoconstrictive mechanisms to treat migraine in patients who have cardiovascular risk factors, stable cardiovascular disease, or those who are dissatisfied with current triptan therapies. Although the efficacy of lasmiditan is expected to be similar to triptans, we believe that rimegepant will differentiate on both durability of efficacy and safety. Rimegepant was well tolerated in the Phase 2b clinical trial, while lasmiditan reported a comparatively high rate of AEs and SAEs in its clinical testing.

### 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 candidate in development is ubrogepant. Ubrogepant is being developed by Allergan and is already in Phase 3 testing, having completed positive Phase 2b trials. Allergan is a global pharmaceutical company with over 16,000 employees and has access to greater financial resources than we do. According to Allergan's annual public filings, it expects product launch of ubrogepant in 2020, which we would expect to precede the potential approval of rimegepant. However, we believe that rimegepant has the potential to be best-in-class based upon the published rimegepant and ubrogepant clinical trial results. Although these agents have not been compared within a single study, the placebo-adjusted outcomes comparing each product candidate's Phase 2b data favor rimegepant on almost all pain and non-pain outcomes compared to ubrogepant.

# Other Acute Treatments for Migraine

Ergot alkaloids (such as Dihydroergotamine (DHE)), analgesics, including opioids, non-steroidal anti-inflammatory drugs, or NSAIDs, acetaminophen and antiemetics also are used in the treatment of migraine. DHE is also a potent vasoconstrictor and has been 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. Botox is the only product that has been approved by the FDA for the prevention of chronic 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. Some other beta blockers, such as atenolol, metoprolol and nadalol are also prescribed off-label for prevention, as well as calcium channel blockers such as diltiazem and tricyclic antidepressants such as amitriptyline.

We believe that BHV-3500 will differentiate from the current anti-CGRP mAbs currently pursuing indications for acute treatment or prevention of, migraine. More specifically, there are currently four anti-CGRP mAbs under clinical development: LY2951742 (developed by Arteaus Therapeutics (USA), with rights subsequently acquired by Eli Lilly and Co.); ALD-403 (developed by Alder Biopharmaceuticals (USA)); LBR-101, now TEV-48125 (developed by Labrys Biologics—Pfizer (USA), then acquired by Teva Pharmaceuticals); and AMG334 (developed by Amgen, Inc. (USA)).

#### **Glutamate Platform**

With respect to trigriluzole, which we are currently developing for the treatment of ataxias, with SCA as our initial indication, 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 IEDAT01, which delivers dexamethasone sodium phosphate through red blood cells, Shinogi & 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 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, which is currently the only approved drug for the treatment of ALS in the United States. Riluzole is also generically available. At least two other companies are marketing or plan to market new formulations of riluzole: MonoSol Rx has filed an IND to begin clinical development of a riluzole oral soluble film, 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 Teglutik. 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.

With respect to BHV-5000, which we are developing for the treatment of breathing irregularities associated with 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 trigriluzole, 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.

### 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.

All of our 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, to commercialize our product candidates in the United States, and we may enter into distribution or licensing arrangements for commercialization rights

for other regions. Members of our management team and board of directors have deep experience leading neuroscience research and have been involved in the development and commercialization of drugs such as Zoloft, Abilify, Opdivo and Soliris.

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 platform, we currently intend to build a neurological specialty sales force to manage orphan drug 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**

Our patent estate, on a worldwide basis, includes 10 families of patents and patent applications which contain claims directed to composition of matter, methods of use or formulations related to our product candidates.

### 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 (BHV-3000), 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. See "—License Agreement with Bristol-Myers Squibb Company" below.

# Trigriluzole

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 trigriluzole and numerous other prodrugs of riluzole. In addition, the use of these compounds for treating ALS, spinocerebellar ataxia, 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, LLC and Fox Chase Chemical Diversity Center, Inc.

See "—Agreement with ALS Biopharma and Fox Chase Chemical Diversity Center" below. If a patent covering trigriluzole 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 currently covered in the United States by several pending U.S. patent applications, with corresponding PCT applications which we intend to nationalize in selected jurisdictions before the applicable deadlines. If a patent covering BHV-0223 issues from one of these pending patent application families, it would have a statutory expiration date in 2035. We have an agreement with Catalent whereby Catalent assigned its rights to a patent application family containing claims directed to the formula for BHV-0223, which is described above, as well as licensed to us certain rights to the Zydis ODT technology. See "—Agreements with Catalent" below. 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. See "—License Agreement with Yale University" below. 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. See "—License Agreement with Rutgers, The State University of New Jersey" below.

### 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. See "—License Agreement with AstraZeneca" below. 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 2019 and the patent applications related to BHV-5000 would, if issued, have a statutory expiration date in 2033.

### 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. See "—License Agreement with The General Hospital Corporation d/b/a Massachusetts General Hospital" below.

# 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, or 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 Bristol-Myers Squibb Company

#### **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 \$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.

Under the BMS agreement, we agreed to refrain, either ourselves or via our sublicensees or third parties, from engaging in the development and commercialization of specified competitive compounds for a period of seven years. Further, BMS has retained the right to use the licensed compounds for internal research purposes and for the generation of analogs and derivatives of licensed compounds. Our right to

sublicense our rights under the BMS agreement, other than to an affiliate or to certain third-party manufacturers, is subject to BMS's prior written consent, which cannot be unreasonably withheld or delayed. While we will be responsible for preparing, prosecuting and maintaining the licensed patents and applications and for defending them in post-grant proceedings, BMS must consent before a licensed patent or application is abandoned in a major jurisdiction. We will also be responsible for listing licensed patents in the Orange Book and for determining which patents will be extended based on any regulatory delays.

# 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 this 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. In satisfaction of this obligation, we expect that we will issue 1,345,374 common shares to BMS in connection with the closing of this offering.

#### Right of First Negotiation

After we receive topline data from a Phase 3 trial of our most advanced product candidate licensed under the agreement, we must provide notice and a summary of the data to BMS. BMS will then have 60 days to exercise its right of first negotiation to regain its intellectual property rights or enter into a license agreement with us with respect to such product candidate. If we do not execute an agreement with BMS during this time period after using good faith efforts, we will have the right to retain our rights or sublicense our rights to third parties subject to the terms of the agreement.

#### 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 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.

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

In August 2015, we entered into an agreement with ALS Biopharma and 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 trigriluzole, 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 trigriluzole 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 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. In connection with the issuance of the warrants, ALS Biopharma became a party to our Shareholders Agreement and, upon achievement of a regulatory milestone, has received board observer rights. We also agreed to grant specified preemptive rights to ALS Biopharma to participate in equity offerings that are open to our other shareholders.

#### 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 trigriluzole 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.

#### License Agreement with AstraZeneca AB

#### **Overview**

In October 2016, we entered into an exclusive license agreement with AstraZeneca 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 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 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. 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 initial public offering. In satisfaction of this obligation, we expect that we will issue an additional 538,149 common shares to AstraZeneca in connection with the closing of this offering.

#### Term and Termination

The agreement 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 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.

### Agreement 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 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.

#### 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 initial public offering, 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 initial public offering, the change-of-control payment to Yale is reduced by the value of Yale's equity investment in our company.

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, or 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.

# **Government Regulation**

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act, or 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 Good Laboratory Practices, or 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, or 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, or 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, or 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 independent institutional review board, or 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 our trigriluzole and BHV-5000 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. We will be required to pay a user fee to the FDA to review the NDA, unless we receive a waiver or qualify for an exemption. This is typically 10 months from the date that the FDA receives the application-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, or 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 user fee requirements for marketed products and the establishments at which such products are manufactured, 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 adverse events 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 trigriluzole 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, or 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 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.

In May 2016, we received orphan drug designation from the FDA for trigriluzole for the treatment of SCA. In December 2016, the FDA granted orphan drug designation for BHV-0223 for the treatment of ALS, with eligibility for orphan drug 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. We intend to seek orphan drug designation and exclusivity for our other product candidates whenever it is available. However, we cannot guarantee that we will obtain orphan drug designation for any other products in any jurisdiction. Even if we are able to obtain orphan drug designation for a product, such as trigriluzole in the treatment of SCA and BHV-0223 in the treatment of ALS, we cannot be sure that such product will be approved, that we will be able to obtain orphan drug exclusivity upon approval, if ever, or that we will be able to maintain any

exclusivity that is granted. In addition, doctors may prescribe products for off-label uses and undermine our exclusivity. Orphan drug exclusivity could also block the approval of one of our products for seven years if a competitor obtains approval for the same active moiety for the same indication before we do, unless we are able to demonstrate that our product is clinically superior.

# 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 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 governmentpaid 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, or 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, or CMS, may develop new payment and delivery models, such as bundled payment models. For example, the U.S. Department of Health and Human Services, or HHS, set a goal of moving 30% of Medicare payments to alternative payment models tied to the quality or value of services by 2016 and 50% of Medicare payments into these alternative payment models by the end of 2018. 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, or 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, or 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, or 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, nondeductible fee on any entity that manufactures or imports certain branded prescription drug agents or biologic agents, which is apportioned among these entities according to their market share in certain government healthcare programs;
- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts to 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;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, unless the drug is subject to discounts under the 340B drug discount program;
- 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;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements under the federal Physician Payments Sunshine Act for drug manufacturers to report information related to payments and other transfers of value made to physicians and teaching hospitals as well as ownership or investment interests held by physicians and their immediate family members;

- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- creation of the Independent Payment Advisory Board, which, if and when impaneled, will have authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs; and
- establishment of a Center for Medicare and Medicaid Innovation at 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. In addition, the current administration and Congress will likely continue to seek legislative and regulatory changes, including repeal and replacement of certain provisions of the ACA. In January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In March 2017, following the passage of the budget resolution for fiscal year 2017, the U.S. House of Representatives introduced legislation known as the American Health Care Act, which, if enacted, would have amended or repealed significant portions of the ACA. However, consensus over the scope and content of the American Health Care Act could not be reached by its proponents in the U.S. House of Representatives. Thus, the proposed legislation has been withdrawn and the prospects for legislative action on this bill are uncertain. Congress could consider other legislation to repeal or replace certain elements of the ACA.

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 has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which have resulted in several recent Congressional inquiries and proposed bills 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.

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

# **Employees**

As of December 31, 2016, we employed 12 employees, and as of February 28, 2017, we employed 18 employees. All of our employees are located in New Haven, Connecticut. None of our employees is represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

#### Facilities

Our principal offices occupy approximately 2,000 square feet of leased office space in New Haven, Connecticut, pursuant to a lease agreement that expires in October 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.

# Legal Proceedings

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 or financial condition.

# MANAGEMENT

# **Directors and Executive Officers**

The following table sets forth information concerning our directors and executive officers, including their ages as of February 28, 2017:

Name	Age	Position
Executive Officers:		
Vlad Coric, M.D.	46	Chief Executive Officer and Director
Robert Berman, M.D.	54	Chief Medical Officer
James Engelhart	53	Chief Financial Officer
John Tilton	49	Chief Commercial Officer
Charles Conway, Ph.D.	55	Chief Scientific Officer
Kimberly Gentile	51	Vice President of Operations
Non-Management Directors:		
Declan Doogan, M.D.	64	Chairman of the Board of Directors
Gregory H. Bailey, M.D.	61	Director
John W. Childs	75	Director
Albert Cha, M.D., Ph.D.	44	Director
Eric Aguiar, M.D.	55	Director

# **Executive Officers**

### Vlad Coric, M.D.

Dr. Coric has served as our chief executive officer and director since October 2015. From January 2007 to September 2015, he served as a group director of global clinical research at Bristol-Myers Squibb Company, focusing both in oncology global clinical research and neuroscience global clinical research. He has been involved in multiple drug development programs including marketed drugs such as Abilify (aripiprazole; partial dopamine agonist), Opdivo (nivolumab; anti-PD1), Yervoy (Ipilimumab; anti-CTLA-4), Daklinza (daclatasvir; NS5A inhibitor) and Sunvepra (asunaprevir; NS3 inhibitor). Since July 2001, Dr. Coric has also continued to serve as an associate clinical professor of psychiatry at Yale School of Medicine. He previously served as the chief of the Yale Clinical Neuroscience Research Unit and the director of the Yale Obsessive-Compulsive Disorder Research Clinic. He has served as president of the Connecticut Psychiatric Society. Dr. Coric received his M.D. from Wake Forest University School of Medicine. He completed his internship at Yale-New Haven Hospital and residency training at the Yale Psychiatry Residency Training Program, where he also served as the program-wide chief resident for the Yale Department of Psychiatry, and chief resident on the PTSD firm at the West-Haven Connecticut Veterans Administration Hospital. Dr. Coric was an honors scholar in neurobiology and physiology at the University of Connecticut where he received a B.S. degree. We believe that Dr. Coric's operational experience with our company gained from serving as our chief executive officer, as well as his extensive experience in the biopharmaceutical industry, qualifies him to serve as a member of our board of directors.

### Robert Berman, M.D.

Dr. Berman has served as our chief medical officer since November 2015. From December 2013 to November 2015, he served as president of Biohaven Medical Services LLC and, prior to that, served as a group director of global clinical research at Bristol-Myers Squibb Company from September 2003 to November 2013. Prior to his time at BMS, Dr. Berman was an associate director of clinical sciences, early development at Pfizer from November 2000 to September 2003. Since October 2012, Dr. Berman has also continued to serve as an adjunct professor of psychiatry at Yale University of Medicine. Dr. Berman

received his B.A. in molecular biophysics and biochemistry from Yale University and his M.D. from Mount Sinai School of Medicine of New York University.

# James Engelhart

Mr. Engelhart has served as our chief financial officer since May 2016. Prior to this, from August 2014 to May 2016, he served as executive director of finance, Americas for Alexion Pharmaceuticals, Inc., and from March 2006 to July 2014, he served as a finance director for Energizer Holdings, Inc. From May 1998 to March 2006, Mr. Engelhart served in increasingly senior finance roles for Bristol-Myers Squibb Company and held finance roles in R&D Operations and International Operations at Schering-Plough from 1992 to 1998. Mr. Engelhart started his career as an auditor with Coopers & Lybrand LLP from 1986 through 1991. Mr. Engelhart received his B.S. in accounting from Villanova University and is a CPA (inactive).

# John Tilton

Mr. Tilton has served as our chief commercial officer since April 2016. Prior to this, from November 2006 to March 2016, he served in increasingly senior marketing and business roles with Alexion Pharmaceuticals, Inc., including serving as its executive director, global sales and marketing operations from January 2011 to March 2016. Prior to Alexion Pharmaceuticals, Mr. Tilton served as a director, division operations at Pfizer from August 2005 to November 2006, as a regional sales manager for Agouron Pharmaceuticals from November 1999 to August 2005 and as division manager at Sanofi from 1993 to 1999. Mr. Tilton received his BSBA in finance from the University of South Carolina-Columbia.

#### Charles Conway, Ph.D.

Dr. Conway has served as our chief scientific officer since January 2017. From January 2000 to January 2017, he held positions of increasing responsibility in drug discovery at Bristol-Myers Squibb Company, or BMS, most recently serving as associate director—biology analytics. Dr. Conway led BMS's biology program efforts working on the CGRP antagonist program for over 10 years and was part of the full development team advancing rimegepant into the clinic. Dr. Conway has extensive experience in the field of pain research and is an inventor on three granted U.S. patents for the treatment of pain. Prior to his time at BMS, Dr. Conway was a postgraduate research anesthesiologist at the University of California San Diego. Dr. Conway received his B.S. in experimental psychology from the University of Central Missouri and his Ph.D. in neuroscience from the University of California Santa Barbara.

#### **Kimberly Gentile**

Ms. Gentile has served as our vice president, clinical operations since February 2014. Before coming to Biohaven, Ms. Gentile served as associate director, project manager, global clinical operations at Bristol-Myers Squibb Company from 2000 to February 2014. Prior to this, she was a senior clinical trial manager at SCIREX Corporation from 1996 to June 2000. Ms. Gentile received her B.S. in Psychology from Salem State University.

# **Non-Management Directors**

# Declan Doogan, M.D.

Dr. Doogan has served as a director of our company since its inception in September 2013. Dr. Doogan has served as the chief executive officer and director of Portage Biotech, Inc. (PTGEF: OTCBB) since June 2013, a director of Portage Pharmaceuticals Limited since July 2013, and a director of Sosei Group Corporation since June 2007. Dr. Doogan has over 30 years of industry experience in both major pharma and biotech. He was the Senior Vice-President and Head of Worldwide Development at Pfizer. He has held a number of executive positions in Pfizer in the US, the UK and Japan. Since leaving

Pfizer in 2007, he has been engaged in executive roles in small pharma. Dr. Doogan was chief medical officer and acting CEO of Amarin (AMRN: NASDAQ). He has also been Chief Medical Officer for Prometheus Laboratories, a molecular diagnostics company in San Diego. Dr. Doogan holds a number of board appointments, principally in pharma companies, and has also held professorship at Harvard School of Public Health, Glasgow University Medical School and Kitasato University (Tokyo). Dr. Doogan received his medical degree from Glasgow University in 1975. He is a Fellow of the Royal College of Physicians and the Faculty of Pharmaceutical Medicine and holds a Doctorate of Science at the University of Kent in the UK. We believe that Dr. Doogan's extensive operational experience in the pharmaceutical and biotech industries qualifies him to serve as a member of our board of directors.

### Gregory H. Bailey, M.D.

Dr. Bailey has served as a director of our company since January 2014. Dr. Bailey is a co-founder and has served as managing partner of MediqVentures since January 2014, the chairman and director of Portage Biotech, Inc. (PTGEF: OTCBB) since June 2013 and a director of Portage Pharmaceuticals Limited since June 2013. He has been a managing partner of Palantir Group, Inc., a merchant bank involved in a number of biotech company startups and financings since April 2002. Dr. Bailey was a founder of SalvaRx Group Plc (LSE: SALV) and has served on its board of directors since May 2015. Dr. Bailey was also the co-founder of Ascent Healthcare Solutions, VirnetX Inc. (VHC:AMEX), Portage Biotech Inc. and DuraMedic Inc. He was the initial financier and an independent director of Medivation, Inc. (MDVN:NASDAQ), from 2005 to December 2012. Dr. Bailey served as the Managing Director and co-Head of Life Sciences at MDB Capital Group LLC from May 2004 to December 2006. Dr. Bailey practiced emergency medicine for ten years before entering finance. He received his medical degree from the University of Western Ontario. We believe that Dr. Bailey's extensive venture capital industry experience and technical background, along with his experience with public companies and biopharmaceutical companies, qualifies him to serve as a member of our board of directors.

### John W. Childs

Mr. Childs has served as a director of our company since January 2014. Mr. Childs has been chairman and partner of J.W. Childs Associates, L.P., a private equity firm, since 1995. From 1991 to 1995, Mr. Childs was senior managing director of Thomas H. Lee Partners and from 1987 to 1990 was a managing director of Thomas H. Lee Partners. Prior to 1987, Mr. Childs was associated with the Prudential Insurance Company of America ("Prudential") for 17 years where he held various executive positions in the investment area, ultimately serving as senior managing director in charge of the Capital Markets Group at which time he was responsible for Prudential's approximately \$77 billion fixed income portfolio, including all of the Capital Markets Group's investments in leveraged acquisitions. He is currently a director and chairman of the board of Sunny Delight Beverages Co., and serves as a director of Esselte Ltd., WS Packaging Group, Inc., and SIMCOM, Inc. Mr. Childs holds a B.A. from Yale University and an M.B.A. from Columbia University. We believe that Mr. Childs' extensive operational and capital markets experience qualifies him to serve as a member of our board of directors.

### Albert Cha, M.D., Ph.D.

Dr. Cha has served as a director of our company since February 2017. In 2000, Dr. Cha joined Vivo Capital, a healthcare investment firm, where he has served in various positions, and he currently serves as a managing partner. He currently serves on the boards of directors of Ascendis Pharma A/S (NASDAQ: ASND), Kalvista Pharmaceuticals (NASDAQ: KALV), and several private companies. Dr. Cha holds B.S. and M.S. degrees in Electrical Engineering from Stanford University and an M.D. degree and Ph.D. degree in Neuroscience from the University of California at Los Angeles. We believe that Dr. Cha's scientific background and experience as an investor in life science companies qualifies him to serve as a member of our board of directors.

# Eric Aguiar, M.D.

Dr. Aguiar has served as a director of our company since February 2017. Dr. Aguiar has been a partner at Aisling Capital since January 2016 and prior to that was a partner at Thomas, McNerney and Partners, a healthcare venture capital and growth equity fund, since 2007. Prior to joining that firm, he was a Managing Director of HealthCare Ventures, a healthcare focused venture capital firm, from 2001 to 2007. Dr. Aguiar currently serves on the board of directors of Invitae Corporation (NYSE: NVTA). Dr. Aguiar is a member of the Board of Overseers of the Tufts School of Medicine and a member of the Council on Foreign Relations. Dr. Aguiar received his medical degree with honors from Harvard Medical School. He graduated with honors from Cornell University as a College Scholar. He was also a Luce Fellow and is a Chartered Financial Analyst. We believe that Dr. Aguiar's medical and finance background and experience as an investor in life science companies qualifies him to serve as a member of our board of directors.

# **Board Composition**

Our board of directors currently consists of six directors. Dr. Doogan is the chairman of the board. There are no family relationships between any of our executive officers and directors.

Each director is currently elected to the board for a one-year term, to serve until the election and qualification of successor directors at the annual meeting of shareholders, or until the director's earlier removal, resignation or death.

Our directors were elected to and currently serve on the board pursuant to a voting agreement among us and several of our largest shareholders. This agreement will terminate upon the closing of this offering, after which there will be no further contractual obligations regarding the election of our directors.

In accordance with our memorandum and articles of association to be in effect upon the closing of this offering, our board of directors will be divided into three classes, each of which will consist, as nearly as possible, of one-third of the total number of directors constituting our entire board and which will serve staggered three-year terms. At each annual meeting of shareholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. Our directors will be divided among the three classes as follows:

- Class I, which will consist of Dr. Aguiar and Dr. Cha, and their term will expire at our first annual meeting of shareholders to be held after the completion of this offering;
- Class II, which will consist of Dr. Bailey and Mr. Childs, and their term will expire at our second annual meeting of shareholders to be held after the completion of this offering; and
- Class III, which will consist of Dr. Coric and Dr. Doogan, and their term will expire at our third annual meeting of shareholders to be held after the completion of this offering.

If the number of directors changes, any increase or decrease will be apportioned among the classes so as to maintain the number of directors in each class as nearly as possible. Any additional directors of a class elected to fill a vacancy resulting from an increase in such class will hold office for a term that coincides with the remaining term of that class. Decreases in the number of directors will not shorten the term of any incumbent director.

These board provisions could make it more difficult for third parties to gain control of our company by making it difficult to replace members of the board of directors.

#### **Director Independence**

Our board of directors has undertaken a review of the independence of the directors and considered whether any director has a material relationship with us that could compromise his ability to exercise

independent judgment in carrying out his responsibilities. As a result of this review, our board of directors has determined that Drs. Doogan, Aguiar and Cha, representing three of our six directors, are "independent directors" as defined under applicable stock exchange rules.

In addition, certain phase-in periods with respect to director independence will be available to us under New York Stock Exchange rules. We do expect to take advantage of certain of these provisions. The phase-in periods allow us to have less than a majority of independent directors upon the listing date of our common shares, so long as our board is majority independent within one year of the effective date of the registration statement.

# **Committees of the Board of Directors**

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee, each of which has the composition and responsibilities described below. From time to time, the board may establish other committees to facilitate the management of our business.

#### Audit Committee

Our audit committee reviews our internal accounting procedures and consults with and reviews the services provided by our independent registered public accountants. Our audit committee consists of three directors, Drs. Aguiar, Cha and Doogan. Dr. Aguiar is the chairman of the audit committee and our board of directors has determined that Dr. Aguiar is an "audit committee financial expert" as defined by SEC rules and regulations. Under Rule 10A-3 under the Exchange Act, we are permitted to phase in our compliance with the independent audit committee requirements set forth in the NYSE rules and Rule 10A-3 under the Exchange Act as follows: one independent member at the time of listing, a majority of independent members within 90 days of listing and all independent members within one year of listing. Our board of directors has determined that each of Drs. Aguiar and Cha is an independent director under New York Stock Exchange listing rules and under Rule 10A-3 under the Exchange Act. As a result, a majority of the members of our audit committee will satisfy the applicable independence requirements of the NYSE rules, and Rule 10A-3 upon the listing of our common shares on the NYSE. We will comply with the phase-in requirements of the NYSE rules, and within one year of our listing on the NYSE, we expect that all members of our audit committee will be independent under NYSE rules and Rule 10A-3. We intend to continue to evaluate the requirements applicable to us and we intend to comply with the future requirements to the extent that they become applicable to our audit committee. The principal duties and responsibilities of our audit committee include:

- appointing and retaining an independent registered public accounting firm to serve as independent auditor to audit our financial statements, overseeing the independent auditor's work and determining the independent auditor's compensation;
- approving in advance all audit services and non-audit services to be provided to us by our independent auditor;
- establishing procedures for the receipt, retention and treatment of complaints received by us regarding accounting, internal accounting controls, auditing or compliance matters, as well as for the confidential, anonymous submission by our employees of concerns regarding questionable accounting or auditing matters;
- reviewing and discussing with management and our independent auditor the results of the annual audit and the independent auditor's review of our quarterly financial statements; and
- conferring with management and our independent auditor about the scope, adequacy and effectiveness of our internal accounting controls, the objectivity of our financial reporting and our accounting policies and practices.

# **Compensation Committee**

Our compensation committee reviews and determines the compensation of our executive officers. Upon completion of this offering, our compensation committee will consist of three directors, Drs. Cha, Aguiar and Doogan, each of whom is a non-employee member of our board of directors as defined in Rule 16b-3 under the Exchange Act. Dr. Cha will be the chairman of the compensation committee. Our board of directors has determined that the composition of our compensation committee satisfies the applicable independence requirements under, and the functioning of our compensation committee complies with the applicable requirements of, the New York Stock Exchange rules and SEC rules and regulations. We intend to continue to evaluate and intend to comply with all future requirements applicable to our compensation committee. The principal duties and responsibilities of our compensation committee will include:

- establishing and approving, and making recommendations to the board of directors regarding, performance goals and objectives relevant to the compensation of our chief executive officer, evaluating the performance of our chief executive officer in light of those goals and objectives and setting, or recommending to the full board of directors for approval, the chief executive officer's compensation, including incentive-based and equity-based compensation, based on that evaluation;
- setting the compensation of our other executive officers, based in part on recommendations of the chief executive officer;
- exercising administrative authority under our stock plans and employee benefit plans;
- establishing policies and making recommendations to our board of directors regarding director compensation;
- reviewing and discussing with management the compensation discussion and analysis that we may be required from time to time to include in SEC filings; and
- preparing a compensation committee report on executive compensation as may be required from time to time to be included in our annual proxy statements or annual reports on Form 10-K filed with the SEC.

# Nominating and Corporate Governance Committee

Upon the completion of this offering, our nominating and corporate governance committee will consist of five directors, Drs. Doogan, Aguiar, Bailey and Cha and Mr. Childs. Dr. Doogan will be the chairman of the nominating and corporate governance committee. Subject to our compliance with the phase-in provisions below, our board of directors has determined that the composition of our nominating and corporate governance committee satisfies the applicable independence requirements under, and the functioning of our nominating and corporate governance committee complies with the applicable requirements of, the New York Stock Exchange standards and SEC rules and regulations. Upon the listing of our common shares on the NYSE, a majority of the members of our nominating and corporate governance committee applicable independence requirements of the NYSE. We are permitted to phase in our compliance with the independent nominating and corporate governance committee requirements of the NYSE. We are permitted to phase in our compliance with the independent nominating and corporate governance committee requirements of the NYSE, which requires all members to be independent within one year of listing. We will comply with the phase-in requirements of the NYSE rules, and within one year of our listing on the NYSE, all members of our nominating and corporate governance committee will be independent under NYSE rules. We will continue to evaluate and will comply with all future requirements applicable to our nominating and corporate governance committee's responsibilities will include:

assessing the need for new directors and identifying individuals qualified to become directors;

- recommending to the board of directors the persons to be nominated for election as directors and to each of the board's committees;
- assessing individual director performance, participation and qualifications;
- developing and recommending to the board corporate governance principles;
- monitoring the effectiveness of the board and the quality of the relationship between management and the board; and
- overseeing an annual evaluation of management's and the board's performance.

#### **Code of Business Conduct and Ethics for Employees, Executive Officers and Directors**

Effective upon the effectiveness of the registration statement of which this prospectus forms a part, we have adopted a Code of Business Conduct and Ethics, or the Code of Conduct, applicable to all of our employees, executive officers and directors. Following the closing of this offering, the Code of Conduct will be available on our website at *www.biohavenpharma.com*. The nominating and corporate governance committee of our board of directors will be responsible for overseeing the Code of Conduct and must approve any waivers of the Code of Conduct for employees, executive officers and directors. We expect that any amendments to the Code of Conduct, or any waivers of its requirements, will be disclosed on our website.

#### **Compensation Committee Interlocks and Insider Participation**

None of our directors who currently serve as members of our compensation committee is, or has at any time during the past year been, one of our officers or employees. None of our executive officers currently serves, or in the past year has served, as a member of the board of directors or compensation committee of any other entity that has one or more executive officers serving on our board of directors or compensation committee.

### **Non-Employee Director Compensation**

We have not historically paid cash retainers or other compensation with respect to service on our board of directors, except for reimbursement of direct expenses incurred in connection with attending meetings of our board of directors or committees of our board of directors. Although prior to this offering we have never had a formal non-employee director compensation policy, we have typically granted stock options to our non-employee directors on an annual basis, as reflected in the tables below under "—2016 Director Compensation Table" and "—Non-Employee Director Equity Outstanding at 2016 Year End."

In April 2017, each of our non-employee directors received an option to purchase 20,000 common shares under the 2014 Plan, except for Dr. Doogan, our chairman, who received an option to purchase 30,000 common shares, each at an exercise price of \$10.82 per share, which was the fair market value of a common share on the date of grant, as determined by our board of directors. Twenty-five percent of the shares underlying each option vested on the date of grant and the remaining shares vest in three equal installments on each of the first, second and third anniversaries of the date of grant, subject to the director's continued service, and will fully vest upon a change in control.

We expect that our board of directors will adopt a director compensation policy for non-employee directors following the closing of this offering.

### **2016 Director Compensation Table**

The following table sets forth information regarding compensation earned for service on our board of directors during the year ended December 31, 2016 by our directors who were not also our employees. Our non-employee directors did not receive any cash compensation for their service on our board of directors

during the year ended December 31, 2016. Dr. Coric, our Chief Executive Officer, is also a director, but does not receive any additional compensation for his service as a director. Dr. Coric's compensation as an executive officer is set forth below under "Executive Compensation—2016 Summary Compensation Table."

	All Other		
Name	Option Awards (\$) <sup>(1)</sup>	Compensation (\$) <sup>(2)</sup>	Total (\$)
Declan Doogan, M.D.	189,428		189,428
Gregory H. Bailey, M.D.	142,829	467,036	609,865
John W. Childs	142,829	467,036	609,865
Kamlesh Shah <sup>(3)</sup>	56,828	—	56,828

- (1) Each director received one option grant during the year ended December 31, 2016 under our 2014 Equity Incentive Plan. A quarter of the shares underlying each option vested upon issuance, and the remaining shares will vest in three equal installments on December 10, 2017, 2018 and 2019, subject to their continued service with us. The amounts in this column reflect the full grant-date fair value for awards granted. The grant-date fair value was computed in accordance with ASC Topic 718, *Compensation—Stock Compensation*. The assumptions we used in valuing options are described in Note 12 to our consolidated financial statements included in this prospectus.
- (2) Represents the fair value of warrants issued to the director in exchange for a guaranty of our obligations under our credit agreement with Wells Fargo. The assumptions we used in valuing warrants are described in Notes 3 and 9 to our consolidated financial statements included in this prospectus.
- (3) Mr. Shah resigned as a director in February 2017.

### Non-Employee Director Equity Outstanding at 2016 Year End

The following table provides information about outstanding stock options and warrants held by each of our non-employee directors as of December 31, 2016. All of the options were granted under our 2014 Equity Incentive Plan.

		Guarantor
Non-Employee Director	Option Awards	Warrants
Declan Doogan, M.D.	475,000(1)	
Gregory H. Bailey, M.D.	400,200(2)	107,500(5)
John W. Childs	400,200(2)	107,500(5)
Kamlesh Shah <sup>(4)</sup>	290,000(3)	

- (1) These option awards consist of three grants: (a) an option to purchase 250,000 common shares, of which 187,500 of the underlying shares have vested and the remaining 62,500 shares will vest in full on November 26, 2017, (b) an option to purchase 175,000 common shares, of which 87,500 of the underlying shares have vested and the remaining 87,500 shares will vest in two equal installments on October 23, 2017 and 2018 and (c) an option to purchase 50,000 common shares, of which 12,500 of the underlying shares have vested and the remaining 37,500 shares will vest in three equal installments on December 10, 2017, 2018 and 2019.
- (2) These option awards consist of three grants: (a) an option to purchase 212,500 common shares, of which 159,375 of the underlying shares have vested and the remaining 53,125 shares will vest in full on November 26, 2017, (b) an option to purchase 150,000 common shares, of which 75,000 of the underlying shares have vested and the remaining 75,000 shares will vest in two equal installments on October 23, 2017 and 2018 and (c) an option to purchase 37,700 common shares, of which 9,425 of the

underlying shares have vested and the remaining 28,275 shares will vest in three equal installments on December 10, 2017, 2018 and 2019.

- (3) These option awards consist of three grants: (a) an option to purchase 212,500 common shares, of which 159,375 of the underlying shares have vested and the remaining 53,125 shares will vest in full on November 26, 2017, (b) an option to purchase 62,500 common shares, of which 31,250 of the underlying shares have vested and the remaining 31,250 shares will vest in two equal installments on October 23, 2017 and 2018 and (c) an option to purchase 15,000 common shares, of which 3,750 of the underlying shares have vested and the remaining 11,250 shares will vest in three equal installments on December 10, 2017, 2018 and 2019.
- (4) Mr. Shah resigned as a director in February 2017.
- (5) We issued a warrant to each of Mr. Childs and Dr. Bailey to purchase 107,500 of our common shares at an exercise price of \$9.2911 per share in exchange for their guaranties relating to our credit agreement with Wells Fargo.

# **EXECUTIVE COMPENSATION**

Our named executive officers for the year ended December 31, 2016 include our principal executive officer and the next two most highly compensated executive officers during the year ended December 31, 2016:

- Vlad Coric, M.D., our chief executive officer;
- Robert Berman, M.D., our chief medical officer; and
- James Engelhart, our chief financial officer.

#### **Summary Compensation Table**

The following table presents the compensation awarded to, earned by or paid to each of our named executive officers for the year ended December 31, 2016.

Name and Principal Position	Year	Salary (\$) <sup>(2)</sup>	Bonus (\$) <sup>(2)(3)</sup>	Option Awards (\$) <sup>(4)</sup>	All Other Compensation (\$) <sup>(2)(5)</sup>	Total (\$)
Vlad Coric, M.D. Chief Executive Officer	2016	350,000	245,000	189,428		784,428
Robert Berman, M.D. <i>Chief Medical Officer</i>	2016	315,000	98,438	102,291	5,331	521,060
James Engelhart Chief Financial Officer	2016	222,592(1)	137,025	118,298	4,908	482,823

- (1) This amount includes \$27,400 paid to Mr. Engelhart for the consulting services he provided to us prior to becoming a full-time employee and executive officer of our company on May 2, 2016. The remaining amount of \$195,192 is the pro-rated amount of Mr. Engelhart's base salary with respect to his services as our chief financial officer for the remainder of 2016.
- (2) These amounts were paid to the executive by Biohaven Pharmaceuticals, Inc., which, as of December 31, 2016, is our wholly owned subsidiary.
- (3) The amounts reflect the discretionary bonus paid for performance during 2016, as discussed further below under "—Narrative to Summary Compensation Table—Annual Bonus."
- (4) The amounts reflect the full grant-date fair value for stock option awards granted during the year ended December 31, 2016 under our 2014 Plan. The grant-date fair value was computed in accordance with ASC Topic 718, *Compensation—Stock Compensation*. The assumptions we used in valuing options are described in Note 12 to our consolidated financial statements included in this prospectus. See "—Narrative to Summary Compensation Table—Long-Term Incentives" below.
- (5) The amounts consist of company contributions to the executive officer's account under our 401(k) plan.

### Narrative to Summary Compensation Table

We review compensation annually for all employees, including our executives. In setting executive base salaries and bonuses and granting equity incentive awards, we consider compensation for comparable positions in the market, the historical compensation levels of our executives, individual performance as compared to our expectations and objectives, our desire to motivate our employees to achieve short- and long-term results that are in the best interests of our shareholders, and a long-term commitment to our company. We do not target a specific competitive position or a specific mix of compensation among base salary, bonus or long-term incentives.

Our board of directors has historically determined our executives' compensation. Our board of directors typically reviews and discusses management's proposed compensation with our chief executive officer for all executives other than our chief executive officer. Based on those discussions and its discretion, our board of directors, without members of management present, discusses and ultimately approves the compensation of our executive officers. To date, our board of directors has not engaged a compensation consultant or adopted a peer group of companies for purposes of determining executive compensation.

#### **Annual Base Salary**

We and our wholly owned subsidiary, Biohaven Pharmaceuticals, Inc., have each entered into employment agreements with each of our named executive officers that establish annual base salaries, which are generally determined, approved and reviewed periodically by our board of directors in order to compensate our named executive officers for the satisfactory performance of duties to our company. Annual base salaries are intended to provide a fixed component of compensation to our named executive officers, reflecting their skill sets, experience, roles and responsibilities. Base salaries for our named executive officers have generally been set by our board of directors at levels deemed necessary to attract and retain individuals with superior talent. The following table presents the base salaries for each of our named executive officers for 2016 and 2017. The 2016 base salaries became effective on January 1, 2016 and the 2017 base salaries became effective on January 1, 2017. Following the completion of this offering, our compensation committee will generally be responsible for approving base salaries for our executive officers.

Name	2016 Annual Base Salary (\$)	2017 Annual Base Salary (\$) <sup>(2)</sup>
Vlad Coric, M.D.	350,000	364,000
Robert Berman, M.D.	315,000	324,450
James Engelhart <sup>(1)</sup>	290,000	301,600

- (1) Mr. Engelhart became an executive officer as of May 2, 2016. His 2016 base salary was pro-rated accordingly.
- (2) In April 2017, our board of directors approved increases in the annual base salaries of our named executive officers, to become effective as of the completion of this offering. Dr. Coric's base salary will increase to \$450,000 and each of Dr. Berman's and Mr. Engelhart's base salaries will increase to \$340,000.

### Annual Bonus

We seek to motivate and reward our executive officers for achievements relative to our corporate goals and expectations for each fiscal year. Each named executive officer has a target bonus opportunity as specified in the officer's respective employment agreement with Biohaven Pharmaceuticals, Inc., defined as a percentage of his annual salary. For 2016, the target bonus was as follows:

Name	2016 Target Bonus (% of Salary)
Vlad Coric, M.D.	35
Robert Berman, M.D.	25
James Engelhart	35

For 2016, our board of directors considered a variety of factors and personal and corporate achievements in determining the discretionary bonus amounts to be paid to each named executive officer.

- With respect to Dr. Coric, the board considered factors such as his involvement in creating value for the company by leading our Series A preferred share financing, negotiating key in-license agreements for our product candidates, recruiting new talent, negotiating and supporting our investment in Kleo Pharmaceuticals, Inc., leading negotiations with other potential collaborators and providing strategy and oversight in the development of our product pipeline.
- With respect to Dr. Berman, the board considered factors such as his involvement in performing key functions and making significant contributions related to our Series A preferred share financing.
- With respect to Mr. Engelhart, the board considered factors such as his establishment of a financial infrastructure for our company and his involvement and contributions related to our Series A preferred share financing and our preparations for this offering.

Based on these factors, in its sole discretion, our board of directors determined to award the following bonuses to each of our named executive officers in December 2016:

Name	2016 Bonus (\$)
Vlad Coric, M.D.	245,000
Robert Berman, M.D.	98,438
James Engelhart	137,025

In April 2017, our board of directors approved the following target bonuses for our executive officers for 2017:

	2017
	Target Bonus
Name	(% of Salary)
Vlad Coric, M.D	50
Robert Berman, M.D	35
James Engelhart	35

#### Long-Term Incentives

Our equity-based incentive awards are designed to align our interests with those of our employees and consultants, including our executive officers. Our board of directors has historically been responsible for approving equity grants, although following the completion of this offering, our compensation committee will generally be responsible for approving equity grants. Vesting of equity awards is generally tied to continuous service with us and serves as an additional retention measure. Our executives generally are awarded an initial new hire grant upon commencement of employment. Additional grants may occur periodically in order to specifically incentivize executives with respect to achieving certain corporate goals or to reward executives for exceptional performance.

Prior to this offering, we have granted all equity awards pursuant to the 2014 Plan, the terms of which are described below under "—Equity Benefit Plans." All options are granted with a per share exercise price equal to no less than the fair market value of a common share on the date of the grant of such award.

In December 2016, our board of directors awarded the following options to purchase common shares to our named executive officers:

Name	Number of Common Shares Underlying Option
Vlad Coric, M.D.	50,000
Robert Berman, M.D.	27,000
James Engelhart	31,225

Each of these options has an exercise price of \$9.2911 per share. Twenty-five percent of the shares underlying each option vested on the date of grant and the remaining shares vest in three equal installments on each of the first, second and third anniversaries of the date of grant, subject to continued employment with us.

In April 2017, our board of directors awarded the following options to purchase common shares to our named executive officers under the 2014 Plan:

	Number of
	Common
	Shares
	Underlying
Name	Option
Vlad Coric, M.D.	40,000
Robert Berman, M.D.	20,000
James Engelhart	40,000

Each of these options has an exercise price of \$10.82 per share, which was the fair market value of a common share on the date of grant, as determined by our board of directors. Twenty-five percent of the shares underlying each option vested on the date of grant and the remaining shares vest in three equal installments on each of the first, second and third anniversaries of the date of grant, subject to continued employment with us, and will fully vest on a change in control.

# **Other Compensation and Benefits**

Except for the benefits described above, we do not provide tax gross-ups, perquisites or personal benefits to our named executive officers. We do, however, pay the premiums for life, medical and dental insurance for all of our employees, including our named executive officers. We also sponsor a tax-qualified 401(k) retirement plan in which our eligible employees are entitled to participate. We match contributions by our employees, including our named executive officers, to our 401(k) plan.

#### **Employment** Agreements

We and our wholly owned subsidiary, Biohaven Pharmaceuticals, Inc., have each entered into employment agreements with each of our named executive officers. Prior to the completion of this offering, the employment agreements between our named executive officers and Biohaven Pharmaceuticals, Inc. are being amended. The key terms of the agreements with our named executive officers, including the expected terms of the amended employment agreements with Biohaven Pharmaceuticals, Inc., are described below. For a discussion of the severance pay and other benefits provided in connection with a termination of employment of our named executive officers, please see "—Payments Upon Termination or Change in Control" below.

### Dr. Coric

We entered into an employment agreement with Dr. Coric, our chief executive officer, in October 2015, and prior to the completion of this offering, Dr. Coric and Biohaven Pharmaceuticals, Inc. are expected to enter into an amended employment agreement. Each of the employment agreements provides for an initial three-year term of employment, with automatic one-year renewal periods, unless either party provides notice of non-renewal at least 90 days before the renewal date. In addition, Dr. Coric's employment is "at-will" and may be terminated at any time by us or Biohaven Pharmaceuticals, Inc., respectively, or Dr. Coric. Under the terms of the amended agreement with Biohaven Pharmaceuticals, Inc., Dr. Coric is expected to be entitled to receive an initial annual base salary of \$450,000, an annual target bonus of 50% of his annual base salary and coverage of the cost to Dr. Coric related to company-sponsored employee benefit plans up to the equivalent of 20% of his annual base salary. The agreements include certain confidentiality, inventions assignment, non-competition and non-solicitation provisions.

# Dr. Berman

We entered into an employment agreement with Dr. Berman, our chief medical officer, in November 2015, and prior to the completion of this offering, Dr. Berman and Biohaven Pharmaceuticals, Inc. are expected to enter into an amended employment agreement. Each of the employment agreements provides for an initial three-year term of employment, with automatic one-year renewal periods, unless either party provides notice of non-renewal at least 90 days before the renewal date. In addition, Dr. Berman's employment is "at-will" and may be terminated at any time by us or Biohaven Pharmaceuticals, Inc., respectively, or Dr. Berman. Under the terms of the amended agreement with Biohaven Pharmaceuticals, Inc., Dr. Berman is expected to be entitled to receive an initial annual base salary of \$340,000, an annual target bonus of 35% of his annual base salary and coverage of the cost to Dr. Berman related to company-sponsored employee benefit plans up to the equivalent of 20% of his annual base salary. The agreements include certain confidentiality, inventions assignment, non-competition and non-solicitation provisions.

#### Mr. Engelhart

We entered into an employment agreement with Mr. Engelhart, our chief financial officer, in May 2016, and prior to the completion of this offering, Mr. Engelhart and Biohaven Pharmaceuticals, Inc. are expected to enter into an amended employment agreement. Each of the employment agreements provides for an initial three-year term of employment, with automatic one-year renewal periods, unless either party provides notice of non-renewal at least 90 days before the renewal date. In addition, Mr. Engelhart's employment is "at-will" and may be terminated at any time by us or Biohaven Pharmaceuticals, Inc., respectively, or Mr. Engelhart. Under the terms of the amended agreement with Biohaven Pharmaceuticals, Inc., Mr. Engelhart is expected to be entitled to receive an initial annual base salary of \$340,000, an annual target bonus of 35% of his annual base salary and coverage of the cost to Mr. Engelhart related to company-sponsored employee benefit plans up to the equivalent of 20% of his annual base salary. The agreements include certain confidentiality, inventions assignment, non-competition and non-solicitation provisions.

#### Payments upon Termination of Employment or Change in Control

Each named executive officer is entitled to severance payments if his employment is terminated under specified circumstances.

### Employment Agreements with Biohaven Pharmaceutical Holding Company Ltd.

Under the employment agreements between us and each of Dr. Coric, Dr. Berman and Mr. Engelhart, if we terminate the executive's employment or fail to elect the executive to his respective officer position, or if the executive's employment is terminated due to death or disability, or if the executive terminates his employment for "Good Reason," the executive is entitled to a lump sum severance payment in the amount of \$350,000 for Dr. Coric, \$157,500 for Dr. Berman and \$290,000 for Mr. Engelhart, and all stock options held by the executive will be deemed to be fully vested and exercisable on the termination date, and the executive may exercise such stock options for a period of two years following the termination date (or if earlier, the end of the term of the option). These severance payments are in addition to any severance payments due to the named executive officers under their agreements with Biohaven Pharmaceuticals, Inc.

# Employment Agreements with Biohaven Pharmaceuticals, Inc.

Under the amended employment agreements between Biohaven Pharmaceuticals, Inc. and each of Dr. Coric, Dr. Berman and Mr. Engelhart, which are expected to be entered into prior to the completion of this offering, if the executive's employment with Biohaven Pharmaceuticals, Inc. is terminated without "just cause," due to death or disability, or if the executive terminates his employment for "Good Reason," each in the absence of a "Change in Control," the executive is entitled to receive severance payments, in equal monthly installments at the applicable base salary rate in effect on the first day of the calendar month immediately preceding the termination date, for 15 months following termination for Dr. Coric, for 12 months following termination for Mr. Engelhart, and for nine months following termination for Dr. Berman. In addition, upon such termination, each executive is entitled to continued health and life insurance coverage during the period during which the executive receives severance payments, reduced to the extent the executive receives comparable benefits elsewhere during the period, all time-based vesting equity awards held by the executive as of the date that he signs the amended employment agreement will be deemed to be fully vested and exercisable on the termination date, and the executive may exercise such awards for a period of two years following the termination date (or if earlier, the end of the term of the option). Upon termination due to disability, the amount of severance paid to the executive is reduced by any disability benefits the executive receives under Biohaven Pharmaceuticals, Inc.'s disability insurance policies.

Under the amended employment agreements between Biohaven Pharmaceuticals, Inc. and each of Dr. Coric, Dr. Berman and Mr. Engelhart, if the executive's employment with Biohaven Pharmaceuticals, Inc. is terminated without "just cause" (not due to death or disability), or if the executive terminates his employment for "Good Reason," each within 12 months following a "Change in Control," the executive will be entitled to receive severance payments, at the applicable base salary rate in effect, and bonus at the full bonus percentage, in equal monthly installments on the first day of the calendar month immediately preceding the termination date, for 18 months following termination for Dr. Coric and for 12 months following termination for Dr. Berman and Mr. Engelhart. In addition, upon such termination, each executive is entitled to continued health and life insurance coverage during the period during which the executive receives severance payments, reduced to the extent the executive receives comparable benefits elsewhere during the period, all time-based vesting equity awards held by the executive as of the date of his termination will be deemed to be fully vested and exercisable on the termination date, and the executive may exercise such awards for the period set forth in his award agreement plus an additional 12 months following the termination date (or if earlier, the end of the term of the award). Upon termination due to disability, the amount of severance paid to the executive is reduced by any disability benefits the executive receives under Biohaven Pharmaceuticals, Inc.'s disability insurance policies.

For purposes of these agreements, "just cause" means the executive's gross negligence, willful misconduct, conviction for a felony (including the entry of a plea of nolo contendere) for illegal or criminal behavior in carrying out his duties as required under the terms of his employment agreement.

For purposes of these agreements, "Good Reason" means the occurrence of any of the following events without the executive's consent: (1) a material reduction in the executive's base salary; (2) a material reduction in the executive's duties, authority and responsibilities relative to the executive's duties, authority, and responsibilities in effect immediately prior to such reduction; (3) the relocation of the executive's principal place of employment, without the executive's consent, in a manner that lengthens his one-way commute distance by 50 or more miles from his then-current principal place of employment immediately prior to such relocation; (4) any material breach of the employment agreement by the applicable of us, Biohaven Pharmaceuticals, Inc. or successors to either entity; or (5) the liquidation, dissolution, merger, consolidation or reorganization of the applicable of us or Biohaven Pharmaceuticals, Inc. or transfer of all or a significant portion of the business and/or assets of either entity, unless the successor or successors shall have assumed all duties and obligations of the applicable of us or Biohaven Pharmaceuticals, Inc. under the employment agreement; provided, however, that, any such termination by the executive shall only be deemed for Good Reason if: (a) the executive gives the applicable of us or Biohaven Pharmaceuticals, Inc. written notice of his intent to terminate for Good Reason within thirty (30) days following the first occurrence of the condition(s) that he believes constitute(s) Good Reason, which notice shall describe such condition(s); (b) the applicable of us or Biohaven Pharmaceuticals, Inc. fails to remedy such condition(s) within thirty (30) days following receipt of the written notice; (c) the applicable of us or Biohaven Pharmaceuticals, Inc. has not, prior to receiving such notice from the executive, already informed the executive that his employment with the applicable of us or Biohaven Pharmaceuticals, Inc. is being terminated and (d) the executive voluntarily terminates his employment within 30 days following the end of the 30-day cure period.

The severance payments described above are in addition to any severance payments due to the named executive officers under their employment agreements with us.

#### **Outstanding Equity Awards at End of 2016**

The following table provides information about outstanding stock options held by each of our named executive officers at December 31, 2016. All of these options were granted under our 2014 Equity Incentive Plan.

	<b>Option</b> Awards			
Name	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price (\$)	Option Expiration Date
Vlad Coric, M.D.	187,500	62,500(1)	0.61	11/26/2024
	50,000	50,000(2)	5.60	10/23/2025
	37,500	37,500(2)	5.60	10/23/2025
	12,500	37,500(3)	9.29	12/10/2026
Robert Berman, M.D.	168,750	56,250(1)	0.61	11/26/2024
	37,500	37,500(2)	5.60	10/23/2025
	37,500	37,500(2)	5.60	10/23/2025
	6,750	20,250(3)	9.29	12/10/2026
James Engelhart	46,875	15,625(1)	0.61	11/26/2024
-	12,500	12,500(2)	5.60	10/23/2025
	7,806	23,419(3)	9.29	12/10/2026

(1) The unvested shares underlying this option vest in full on November 26, 2017, subject to the officer's continued service through such vesting date.

- (2) The unvested shares underlying this option vest in two equal installments on October 23, 2017 and 2018, subject to the officer's continued service through each applicable vesting date.
- (3) The unvested shares underlying this option vest in three equal installments on December 10, 2017, 2018 and 2019, subject to the officer's continued service through each applicable vesting date.

### **Stock Option Exercises and Stock Vested During 2016**

None of our named executive officers exercised stock options during 2016 or held stock awards that vested in 2016.

#### **Pension Benefits**

Other than our 401(k) plan, our named executive officers did not participate in, or otherwise receive any benefits under, any pension or retirement plan sponsored by us during 2016.

# **Nonqualified Deferred Compensation**

Our named executive officers did not participate in, or otherwise receive any benefits under, any nonqualified deferred compensation plan sponsored by us during 2016.

#### **Equity Benefit Plans**

#### 2017 Equity Incentive Plan

Our board of directors adopted our 2017 Equity Incentive Plan, or 2017 Plan, in April 2017, and our shareholders have approved the 2017 Plan. The 2017 Plan became effective as of the date of the underwriting agreement in connection with this offering. Upon the effectiveness of the 2017 Plan, no further grants will be made under the 2014 Plan.

*Share Awards.* The 2017 Plan provides for the grant of incentive share options, or ISOs, nonstatutory share options, or NSOs, share appreciation rights, restricted share awards, restricted share unit awards, performance-based share awards, and other forms of equity compensation, which we refer to collectively as share awards. Additionally, the 2017 Plan provides for the grant of performance cash awards. ISOs may be granted only to employees. All other awards may be granted to employees, including officers, and to non-employee directors and consultants of us and our affiliates.

*Share Reserve.* Initially, the aggregate number of common shares that may be issued pursuant to share awards under the 2017 Plan after the 2017 Plan becomes effective is 7,611,971 shares which is the sum of (1) 2,712,741 new shares, plus (2) the number of shares reserved for issuance under the 2014 Plan, plus (3) any shares subject to outstanding share awards that would have otherwise been returned to the 2014 Plan. Additionally, the number of common shares reserved for issuance under our 2017 Plan may be increased by our board of directors on January 1 of each year, beginning on January 1, 2018 and continuing through and including January 1, 2027, by a number of common shares outstanding on December 31 of the preceding calendar year.

Section 162(m) Limits. No person may be granted share awards covering more than 3,000,000 common shares under our 2017 Plan during any calendar year pursuant to share options, share appreciation rights and other share awards whose value is determined by reference to an increase over an exercise or strike price of at least 100% of the fair market value on the date the share award is granted. Additionally, no person may be granted in a calendar year a performance share award covering more than 3,000,000 shares or a performance cash award having a maximum value in excess of \$3,000,000. Such limitations are designed to help assure that any deductions to which we would otherwise be entitled with

respect to such awards will not be subject to the \$1,000,000 limitation on the income tax deductibility of compensation paid to any covered executive officer imposed by Section 162(m) of the Code.

*Reversion of Shares.* If a share award granted under the 2017 Plan expires or otherwise terminates without being exercised in full, or is settled in cash, the common shares not acquired pursuant to the share award again will become available for subsequent issuance under the 2017 Plan. In addition, the following types of shares under the 2017 Plan may become available for the grant of new share awards under the 2017 Plan: (1) shares that are forfeited to or repurchased by us prior to becoming fully vested; (2) shares withheld to satisfy income or employment withholding taxes; or (3) shares used to pay the exercise or purchase price of a share award. Shares issued under the 2017 Plan may be previously unissued shares or reacquired shares bought by us on the open market. As of the date hereof, no awards have been granted and no common shares have been issued under the 2017 Plan.

*Non-Employee Director Compensation Limit.* Under the 2017 Plan, the maximum number of common shares subject to share awards granted under the 2017 Plan or otherwise during any one calendar year to any of our non-employee directors, taken together with any cash fees paid by us to such non-employee director during such calendar year for services on the board of directors, will not exceed \$1,000,000 in total value (calculating the value of any such share awards based on the grant date fair value of such share awards for financial reporting purposes).

*Administration.* Our board of directors, or a duly authorized committee thereof, has the authority to administer the 2017 Plan. Our board of directors may also delegate to one or more of our officers the authority to (1) designate employees (other than other officers) to be recipients of certain share awards, and (2) determine the number of common shares to be subject to such share awards. Subject to the terms of the 2017 Plan, our board of directors or the authorized committee, referred to herein as the plan administrator, determines recipients, dates of grant, the numbers and types of share awards to be granted and the terms and conditions of the share awards, including the period of their exercisability and vesting schedule applicable to a share award. Subject to the limitations set forth below, the plan administrator will also determine the exercise price, strike price or purchase price of awards granted and the types of consideration to be paid for the award.

The plan administrator has the authority to modify outstanding awards under our 2017 Plan. Subject to the terms of our 2017 Plan, the plan administrator has the authority to reduce the exercise, purchase or strike price of any outstanding share award, cancel any outstanding share award in exchange for new share awards, cash or other consideration, or take any other action that is treated as a repricing under generally accepted accounting principles, with the consent of any adversely affected participant.

*Share Options.* ISOs and NSOs are granted pursuant to share option agreements adopted by the plan administrator. The plan administrator determines the exercise price for a share option, within the terms and conditions of the 2017 Plan, provided that the exercise price of a share option generally cannot be less than 100% of the fair market value of our common shares on the date of grant. Options granted under the 2017 Plan vest at the rate specified by the plan administrator.

The plan administrator determines the term of share options granted under the 2017 Plan, up to a maximum of 10 years. Unless the terms of an optionholder's share option agreement provide otherwise, if an optionholder's service relationship with us, or any of our affiliates, ceases for any reason other than disability or death, the optionholder may generally exercise any vested options for a period of 3 months following the cessation of service. The option term may be extended in the event that exercise of the option following such a termination of service is prohibited by applicable securities laws or our insider trading policy. If an optionholder's service relationship with us or any of our affiliates ceases due to disability or death, or an optionholder dies within a certain period following cessation of service, the optionholder or a beneficiary may generally exercise any vested options for a period of 12 months in the event of disability

and 18 months in the event of death. In no event may an option be exercised beyond the expiration of its term.

Acceptable consideration for the purchase of common shares issued upon the exercise of a share option will be determined by the plan administrator and may include (1) cash, check, bank draft or money order, (2) a broker-assisted cashless exercise, (3) the tender of common shares previously owned by the optionholder, (4) a net exercise of the option if it is an NSO, and (5) other legal consideration approved by the plan administrator.

Unless the plan administrator provides otherwise, options generally are not transferable except by will, the laws of descent and distribution, or pursuant to a domestic relations order. An optionholder may designate a beneficiary, however, who may exercise the option following the optionholder's death.

*Tax Limitations on Incentive Share Options.* The aggregate fair market value, determined at the time of grant, of our common shares with respect to ISOs that are exercisable for the first time by an optionholder during any calendar year under all of our share plans and the share plans of any of our affiliates may not exceed \$100,000. Options or portions thereof that exceed such limit will generally be treated as NSOs. No ISO may be granted to any person who, at the time of the grant, owns or is deemed to own shares possessing more than 10% of our total combined voting power or that of any of our affiliates unless (1) the option exercise price is at least 110% of the fair market value of the shares subject to the option on the date of grant, and (2) the term of the ISO does not exceed five years from the date of grant.

*Restricted Share Awards.* Restricted share awards are granted pursuant to restricted share award agreements adopted by the plan administrator. Restricted share awards may be granted in consideration for (1) cash, check, bank draft or money order, (2) services rendered to us or our affiliates, or (3) any other form of legal consideration. Common shares acquired under a restricted share award may, but need not, be subject to a share repurchase option in our favor in accordance with a vesting schedule to be determined by the plan administrator. A restricted share award may be transferred only upon such terms and conditions as set by the plan administrator. Except as otherwise provided in the applicable award agreement, restricted shares that have not vested will be forfeited or repurchased by us upon the participant's cessation of continuous service for any reason.

*Restricted Share Unit Awards.* Restricted share unit awards are granted pursuant to restricted share unit award agreements adopted by the plan administrator. Restricted share unit awards may be granted in consideration for any form of legal consideration. A restricted share unit award may be settled by cash, delivery of shares, a combination of cash and shares as deemed appropriate by the plan administrator, or in any other form of consideration set forth in the restricted share unit award agreement. Additionally, dividend equivalents may be credited in respect of shares covered by a restricted share unit award. Except as otherwise provided in the applicable award agreement, restricted share units that have not vested will be forfeited upon the participant's cessation of continuous service for any reason.

*Share Appreciation Rights.* Share appreciation rights are granted pursuant to share appreciation grant agreements adopted by the plan administrator. The plan administrator determines the strike price for a share appreciation right, which generally cannot be less than 100% of the fair market value of our common shares on the date of grant. Upon the exercise of a share appreciation right, we will pay the participant an amount equal to the product of (1) the excess of the per share fair market value of our common shares on the date of exercise over the strike price, multiplied by (2) the number of common shares with respect to which the share appreciation right agreement as determined by the plan administrator.

The plan administrator determines the term of share appreciation rights granted under the 2017 Plan, up to a maximum of 10 years. Unless the terms of a participant's share appreciation right agreement provides otherwise, if a participant's service relationship with us or any of our affiliates ceases for any



reason other than disability or death, the participant may generally exercise any vested share appreciation right for a period of 3 months following the cessation of service. The share appreciation right term may be further extended in the event that exercise of the share appreciation right following such a termination of service is prohibited by applicable securities laws. If a participant's service relationship with us, or any of our affiliates, ceases due to disability or death, or a participant dies within a certain period following cessation of service, the participant or a beneficiary may generally exercise any vested share appreciation right for a period of 12 months in the event of disability and 18 months in the event of death. In no event may a share appreciation right be exercised beyond the expiration of its term.

*Performance Awards.* The 2017 Plan permits the grant of performance-based share and cash awards that may qualify as performance-based compensation that is not subject to the \$1,000,000 limitation on the income tax deductibility of compensation paid to a covered executive officer imposed by Section 162(m) of the Code. To help assure that the compensation attributable to performance-based awards will so qualify, our compensation committee can structure such awards so that shares or cash will be issued or paid pursuant to such award only after the achievement of certain pre-established performance goals during a designated performance period.

The performance goals that may be selected include one or more of the following: (1) earnings (including earnings per share and net earnings); (2) earnings before interest and taxes; (3) earnings before interest, taxes and depreciation; (4) earnings before interest, taxes, depreciation and/or amortization; (5) earnings before interest, taxes, depreciation, amortization and legal settlements; (6) earnings before interest, taxes, depreciation, amortization, legal settlements and other income (expense); (7) earnings before interest, taxes, depreciation, amortization, legal settlements, other income (expense) and share-based compensation; (8) earnings before interest, taxes, depreciation, amortization, legal settlements, other income (expense), share-based compensation and changes in deferred revenue; (9) earnings before interest, taxes, depreciation, amortization, legal settlements, other income (expense), share-based compensation, other non-cash expenses and changes in deferred revenue; (10) total shareholder return; (11) return on equity or average shareholders' equity; (12) return on assets, investment, or capital employed; (13) return on operating revenue; (14) margin (including gross margin); (15) income (before or after taxes); (16) operating income (before or after taxes); (17) operating income after taxes; (18) operating income before interest and taxes; (19) operating income before interest, taxes, depreciation and amortization; (20) pre-tax profit; (21) operating cash flow; (22) sales or revenue targets; (23) increases in revenue or product revenue; (24) improvement in or attainment of working capital levels; (25) economic value added (or an equivalent metric); (26) cash flow; (27) cash flow per share; (28) cash balance; (29) cash burn; (30) cash collections; (31) debt reduction; (32) implementation or completion of projects or processes (including, without limitation, clinical trial initiation, clinical trial enrollment and dates, clinical trial results, regulatory filing submissions, regulatory filing acceptances, regulatory or advisory committee interactions, regulatory approvals, and product supply); (33) shareholders' equity; (34) capital expenditures; (35) debt levels; (36) operating profit or net operating profit; (37) workforce diversity; (38) net income or growth of net income or operating income; (39) billings; (40) bookings; (41) employee retention; (42) initiation of studies by specific dates; (43) budget management; (44) submission to, or approval by, a regulatory body (including, but not limited to the U.S. Food and Drug Administration) of an applicable filing or a product; (45) regulatory milestones; (46) safety performance; (47) sustainability or environmental performance; (48) progress of internal research or development programs; (49) acquisition of new customers; (50) customer retention and/or repeat order rate; (51) improvements in sample and test processing times; (52) progress of partnered programs; (53) partner satisfaction; (54) timely completion of clinical trials; (55) submission of 510(k)s or pre-market approvals and other regulatory achievements; (56) milestones related to research development (including, but not limited to, preclinical and clinical studies), product development and manufacturing or new product innovation; (57) expansion of sales in additional geographies or markets; (58) research progress, including the development of programs; (59) strategic partnerships or transactions (including in-licensing and out-licensing of intellectual property; (60) strategic corporate objectives relating to: increase in revenue with certain customers, customer groups,

or customer types; (61) financings; (62) brand recognition or acceptance; (63) share price; (64) share price performance; (65) market share; (66) expenses and cost reduction goals and (67) to the extent that an award is not intended to comply with Section 162(m) of the Code, other measures of performance selected by our board of directors. The performance goals may be based on a company-wide basis, with respect to one or more business units, divisions, affiliates, or business segments, and in either absolute terms or relative to the performance of one or more comparable companies or the performance of one or more relevant indices. Unless specified otherwise (1) in the award agreement at the time the award is granted or (2) in such other document setting forth the performance goals at the time the goals are established, we will appropriately make adjustments in the method of calculating the attainment of performance goals as follows: (a) to exclude restructuring and/or other nonrecurring charges; (b) to exclude exchange rate effects; (c) to exclude the effects of changes to generally accepted accounting principles; (d) to exclude the effects of any statutory adjustments to corporate tax rates; (e) to exclude the effects of any items that are unusual in nature or occur infrequently as determined under generally accepted accounting principles; (f) to exclude the dilutive effects of acquisitions or joint ventures; (g) to assume that any business divested by us achieved performance objectives at targeted levels during the balance of a performance period following such divestiture; (h) to exclude the effect of any change in the outstanding common shares by reason of any share dividend or split, share repurchase, reorganization, recapitalization, merger, consolidation, spin-off, combination or exchange of shares or other similar corporate change, or any distributions to common shareholders other than regular cash dividends; (i) to exclude the effects of share based compensation and the award of bonuses under our bonus plans; (j) to exclude costs incurred in connection with potential acquisitions or divestitures that are required to be expensed under generally accepted accounting principles; (k) to exclude the goodwill and intangible asset impairment charges that are required to be recorded under generally accepted accounting principles; (1) to exclude the effect of any other unusual, non-recurring gain or loss or other extraordinary item; and (m) to exclude the effects of the timing of acceptance for review and/or approval of submissions to the FDA or any other regulatory body. In addition, we retain the discretion to reduce or eliminate the compensation or economic benefit due upon attainment of the goals. The performance goals may differ from participant to participant and from award to award.

*Other Share Awards.* The plan administrator may grant other awards based in whole or in part by reference to our common shares. The plan administrator will set the number of shares under the share award and all other terms and conditions of such awards.

*Changes to Capital Structure.* In the event that there is a specified type of change in our capital structure, such as a share split or recapitalization, appropriate adjustments will be made to (1) the class and maximum number of shares reserved for issuance under the 2017 Plan, (2) the class and maximum number of shares by which the share reserve may increase automatically each year, (3) the class and maximum number of shares that may be issued upon the exercise of ISOs, (4) the class and maximum number of shares subject to share awards that can be granted in a calendar year (as established under the 2017 Plan pursuant to Section 162(m) of the Code) and (5) the class and number of shares and exercise price, strike price, or purchase price, if applicable, of all outstanding share awards.

*Corporate Transactions.* In the event of certain specified significant corporate transactions, the plan administrator has the discretion to take any of the following actions with respect to share awards:

- arrange for the assumption, continuation or substitution of a share award by a surviving or acquiring entity or parent company;
- arrange for the assignment of any reacquisition or repurchase rights held by us to the surviving or acquiring entity or parent company;
- accelerate the vesting of the share award and provide for its termination prior to the effective time of the corporate transaction;

- arrange for the lapse of any reacquisition or repurchase right held by us;
- cancel or arrange for the cancellation of the share award in exchange for such cash consideration, if any, as our board of directors may deem appropriate; or
- make a payment equal to the excess of (a) the value of the property the participant would have received upon exercise of the share award over (b) the exercise price otherwise payable in connection with the share award, provided that the payment may be \$0 if the value of the property is equal to or less than the exercise price, and payments may be delayed to the same extent that payment of consideration to the holders of common shares in connection with the corporate transaction is delayed as a result of escrows, earn outs, holdbacks or other contingencies.

Our plan administrator is not obligated to treat all share awards, even those that are of the same type, in the same manner.

Under the 2017 Plan, a corporate transaction is generally the consummation of (1) a sale or other disposition of all or substantially all of our assets, (2) a sale or other disposition of at least 50% of our outstanding securities, (3) a merger, consolidation or similar transaction following which we are not the surviving corporation, or (4) a merger, consolidation or similar transaction following which we are the surviving corporation but the common shares outstanding immediately prior to such transaction are converted or exchanged into other property by virtue of the transaction.

*Change in Control.* In the event that the surviving corporation or successor corporation (or its parent company) in a change in control transaction does not assume or substitute for any outstanding share award held by any participant whose continuous service has not terminated before the effective time of the change in control, then contingent upon the closing of the transaction, the participant will fully vest in and, to the extent applicable, have the right to exercise all of his or her share awards. In addition, all restrictions on share awards will lapse, and, with respect to any share award with performance-based vesting, all performance goals or other vesting criteria will be deemed achieved at 100% of target levels and all other terms and conditions met. Unless otherwise determined by our board of directors, we will notify the participant in writing or electronically that any options or share appreciation rights held by the participant with accelerated vesting will be exercisable for a period of time determined by the board in its sole discretion, and the options or share appreciation rights will terminate upon the expiration of that period. In addition, the plan administrator may provide, in an individual award agreement or in any other written agreement between a participant and us that the share award will be subject to additional acceleration of vesting and exercisability in the event of a change in control. Under the 2017 Plan, a change in control is generally (1) the acquisition by a person or entity of more than 50% of our combined voting power other than by merger, consolidation or similar transaction; (2) a consummated merger, consolidation or similar transaction immediately after which our shareholders cease to own more than 50% of the combined voting power of the surviving entity; (3) a consummated sale, lease or exclusive license or other disposition of all or substantially of our assets; (4) a complete dissolution or liquidation of the Company, except for a liquidation into a parent corporation, or (5) when a majority of our board of directors becomes comprised of individuals who were not serving on our board of directors on the date of adoption of the 2017 Plan, or the incumbent board, or whose nomination, appointment, or election was not approved by a majority of the incumbent board still in office.

*Amendment and Termination.* Our board of directors has the authority to amend, suspend, or terminate our 2017 Plan, provided that such action does not materially impair the existing rights of any participant without such participant's written consent. No ISOs may be granted after the 10th anniversary of the date our board of directors adopted our 2017 Plan.

# 2014 Equity Incentive Plan

Our board of directors adopted and our shareholders approved our 2014 Equity Incentive Plan, or 2014 Plan, on November 24, 2014. The 2014 Plan was subsequently amended by our board of directors, most recently as of October 28, 2016. As of February 28, 2017, options to purchase 4,335,344 common shares were outstanding under the 2014 Plan, with a weighted average exercise price per share of \$4.23. As of April 24, 2017, 372 shares remained available for future issuance pursuant to the grant of options or other share awards under the 2014 Plan. After the effective date of the 2017 Plan, no additional share awards will be granted under the 2014 Plan, and all outstanding share awards granted under the 2014 Plan that are repurchased, forfeited, expired or are cancelled will become available for grant under the 2017 Plan in accordance with its terms.

*Share Awards.* The 2014 Plan provides for the grant of incentive share options, or ISOs, nonqualified share options, or NSOs, restricted share awards and other share-based awards. ISOs may be granted only to employees. NSOs, restricted share awards and other share-based awards may be granted to directors, officers and employees of the company. We have only granted share options under the 2014 Plan.

*Share Reserve.* The aggregate number of common shares reserved for issuance pursuant to share awards under the 2014 Plan is 4,889,230 shares. The maximum number of shares that may be issued upon the exercise of ISOs under our 2014 Plan is 4,889,230 shares. These amounts are subject to adjustment for share splits, share dividends and other changes in our capital structure. We may use authorized and unissued shares or reacquired shares in connection with grants under the 2014 Plan. Shares underlying the unexercised or undistributed portion of any terminated or expired award are available for further awards under the 2014 Plan.

*Administration.* The compensation committee of our board of directors (or if no compensation committee, the board) has the authority to administer the 2014 Plan. Subject to the terms of the 2014 Plan, the plan administrator determines recipients of awards, dates of grant, the purchase price of shares subject to awards, whether each option is a NSO or ISO, the numbers and types of awards to be granted and the terms and conditions of awards, including the period of their exercisability, the forms of award agreements and vesting schedule applicable to an award. The plan administrator has the authority to interpret and prescribe and rescind rules and regulations and make all other determinations regarding the administration of the 2014 Plan. The plan administrator has the authority to modify, amend or terminate outstanding share awards under our 2014 Plan, including substituting another award of the same or a different type and changing the date of exercise or vesting, provided that the participant's consent will be required unless the plan administrator determines that the action would not materially adversely affect the participant.

*Share Options.* ISOs and NSOs are granted pursuant to share option agreements adopted by the plan administrator. The plan administrator determines the exercise price for a share option, within the terms and conditions of the 2014 Plan, provided that the exercise price of a share option cannot be less than 100% of the fair market value of our common shares on the date of grant. Options granted under the 2014 Plan vest at the rate specified by the plan administrator.

The plan administrator determines the term of share options granted under the 2014 Plan, up to a maximum of 10 years. Unless the terms of an optionholder's share option agreement provide otherwise, an option will terminate 30 days following cessation of the optionholder's service with us or an affiliate for any reason other than cause, death or disability, immediately upon cessation of service for cause, or one year following cessation of service due to death or disability. Acceptable consideration for the purchase of common shares issued upon the exercise of a share option will be determined by the plan administrator, in its discretion, and may include (1) cash or a check, (2) a promissory note, to the extent permitted by applicable law, (3) consideration received under a cashless exercise program, (4) the tender of common shares previously owned by the optionholder, (5) net exercise or (6) any combination of these methods.

Unless the plan administrator provides otherwise, options generally are not transferable except by will or the laws of descent and distribution.

*Tax Limitations On Incentive Share Options.* The aggregate fair market value, determined at the time of grant, of our common shares with respect to ISOs that are exercisable for the first time by an optionholder during any calendar year under all of our share plans may not exceed \$100,000. Options or portions thereof that exceed such limit will generally be treated as NSOs. No ISO may be granted to any person who, at the time of the grant, owns or is deemed to own shares possessing more than 10% of our total combined voting power or that of any of our affiliates unless (1) the option exercise price is at least 110% of the fair market value of the shares subject to the option on the date of grant, and (2) the option is not exercisable after the expiration of five years from the date of grant.

*Changes to Capital Structure.* In the event that there is a specified type of change in our capital structure, such as a recapitalization, reorganization or share split, appropriate adjustments will be made to the number and class of shares that may be delivered under the 2014 Plan, and/or the number, class and price of shares covered by each outstanding share award.

*Change in Control.* In the event of certain change-in-control transactions affecting us (as described below), subject to the provisions of the applicable award agreement, the plan administrator may, in its discretion, provide that all outstanding unvested options will vest and become exercisable and any restrictions applicable to any restricted share awards will terminate and lapse immediately prior to the consummation of the change in control. In addition, the plan administrator has the discretion to take any of the following actions with respect to share awards:

- upon written notice, provide that any outstanding options must be exercised, to the extent then exercisable, within a specified number of days after the date of notice, at the end of which the options will terminate;
- if there is a surviving or acquiring entity, subject to the consummation of the transaction, cause that entity or its affiliate to grant replacement awards having such terms and conditions as the plan administrator determines to be appropriate in its sole discretion, and terminate and cancel the original awards upon replacement;
- terminate any outstanding options, or repurchase any restricted share awards, in exchange for such amounts as the plan administrator determines appropriate in its sole discretion; or
- any combination of the foregoing actions.

For purposes of the treatment above, a "change in control" generally means a single transaction or series of related transactions, other than an initial public offering of our shares, pursuant to which a person or persons unaffiliated with us, other than our existing shareholders:

- acquires shares possessing the voting power to elect a majority of the members of our board of directors;
- consummate a merger, amalgamation or consolidation with us as a result of which the holders of our common shares or other voting securities prior to the transaction(s) own, directly or indirectly, less than 50% of the voting securities of the surviving entity; or
- acquire all or substantially all of our assets.

Our plan administrator is not obligated to treat all share awards, all share awards held by a participant, or all share awards of the same type, in the same manner.

*Amendment and Termination.* The 2014 Plan will terminate on the tenth anniversary of the date it was adopted by our board of directors. However, our board of directors has the authority to amend, suspend, or terminate our 2014 Plan in whole or in part at any time, provided that any amendment that is

necessary to comply with any applicable tax or regulatory requirement will be subject to approval by our shareholders, and such action does not materially adversely affect the existing rights of any participant without such participant's written consent.

### 2017 Employee Share Purchase Plan

Our board of directors adopted our 2017 Employee Share Purchase Plan, or ESPP, in April 2017, and our shareholders have approved the ESPP. The ESPP became effective upon the execution and delivery of the underwriting agreement related to this offering. The purpose of the ESPP is to secure the services of new employees, to retain the services of existing employees and to provide incentives for such individuals to exert maximum efforts toward our success and that of our affiliates. The ESPP is intended to qualify as an "employee stock purchase plan" within the meaning of Section 423 of the Code.

*Share Reserve.* The ESPP authorizes the issuance of 339,139 common shares pursuant to purchase rights granted to our employees or to employees of any of our designated affiliates. The number of common shares reserved for issuance will automatically increase on January 1 of each calendar year, from January 1, 2018 through January 1, 2027, by the lesser of (1) 1% of the total number of common shares outstanding on December 31 of the preceding calendar year, and (2) 600,000 shares; *provided*, that prior to the date of any such increase, our board of directors may determine that such increase will be less than the amount set forth in clauses (1) and (2). As of the date hereof, no common shares have been purchased under the ESPP.

*Administration.* Our board of directors has delegated concurrent authority to administer the ESPP to our compensation committee. The ESPP is implemented through a series of offerings under which eligible employees are granted purchase rights to purchase common shares on specified dates during such offerings. Under the ESPP, we may specify offerings with durations of not more than 27 months, and may specify shorter purchase periods within each offering. Each offering will have one or more purchase dates on which common shares will be purchased for employees participating in the offering. An offering under the ESPP may be terminated under certain circumstances.

*Payroll Deductions.* Generally, all regular employees, including executive officers, employed by us or by any of our designated affiliates, may participate in the ESPP and may contribute, normally through payroll deductions, up to 15% of their earnings (as defined in the ESPP) for the purchase of our common shares under the ESPP. Unless otherwise determined by our board of directors, common shares will be purchased for the accounts of employees participating in the ESPP at a price per share equal to the lower of (a) 85% of the fair market value of a common share on the first date of an offering or (b) 85% of the fair market value of a common share on the date of purchase.

*Limitations.* Employees may have to satisfy one or more of the following service requirements before participating in the ESPP, as determined by our board of directors, including: (1) being customarily employed for more than 20 hours per week; (2) being customarily employed for more than five months per calendar year; or (3) continuous employment with us or one of our affiliates for a period of time (not to exceed two years). No employee may purchase shares under the ESPP at a rate in excess of \$25,000 worth of our common shares based on the fair market value per common share at the beginning of an offering for each year such a purchase right is outstanding. Finally, no employee will be eligible for the grant of any purchase rights under the ESPP if immediately after such rights are granted, such employee has voting power over 5% or more of our outstanding capital stock measured by vote or value pursuant to Section 424(d) of the Code.

*Changes to Capital Structure.* In the event that there occurs a change in our capital structure through such actions as a stock split, merger, consolidation, reorganization, recapitalization, reincorporation, stock dividend, dividend in property other than cash, large nonrecurring cash dividend, liquidating dividend, combination of shares, exchange of shares, change in corporate structure or similar transaction, the board

of directors will make appropriate adjustments to (1) the number of shares reserved under the ESPP, (2) the maximum number of shares by which the share reserve may increase automatically each year, (3) the number of shares and purchase price of all outstanding purchase rights, and (4) the number of shares that are subject to purchase limits under ongoing offerings.

*Corporate Transactions.* In the event of certain significant corporate transactions, including: (1) a sale of all or substantially all of our assets, (2) the sale or disposition of 50% of our outstanding securities, (3) the consummation of a merger or consolidation where we do not survive the transactions and (4) the consummation of a merger or consolidation where we do survive the transaction but the common shares outstanding immediately prior to such transaction are converted or exchanged into other property by virtue of the transaction, any then-outstanding rights to purchase our shares under the ESPP may be assumed, continued or substituted for by any surviving or acquiring entity (or its parent company). If the surviving or acquiring entity (or its parent company) elects not to assume, continue or substitute for such purchase rights, then the participants' accumulated payroll contributions will be used to purchase common shares within 10 business days prior to such corporate transaction, and such purchase rights will terminate immediately.

*ESPP Amendments, Termination.* Our board of directors has the authority to amend or terminate our ESPP, provided that except in certain circumstances such amendment or termination may not materially impair any outstanding purchase rights without the holder's consent. We will obtain shareholder approval of any amendment to our ESPP as required by applicable law or listing requirements.

#### Limitation of Liability and Indemnification of Officers and Directors

We have adopted amended memorandum and articles of association, to be effective following this offering, which will contain provisions that limit the liability of our directors for monetary damages to the fullest extent permitted by British Virgin Islands law.

Any amendment to, or repeal of, these provisions will not eliminate or reduce the effect of these provisions in respect of any act, omission or claim that occurred or arose prior to that amendment or repeal.

The amended memorandum and articles of association provide that we will indemnify, to the fullest extent permitted by law, any person who is or was a party or is threatened to be made a party to any action, suit or proceeding by reason of the fact that he is or was one of our directors or officers or is or was serving at our request as a director or officer of another corporation, partnership, joint venture, trust, or other enterprise. The amended memorandum and articles of association will also provide that we may indemnify to the fullest extent permitted by law any person who is or was a party or is threatened to be made a party to any action, suit, or proceeding by reason of the fact that he is or was one of our employees or agents or is or was serving at our request as an employee or agent of another corporation, partnership, joint venture, trust, or other enterprise. Our amended memorandum and articles of association will also provide that we must advance expenses incurred by or on behalf of a director or officer in advance of the final disposition of any action or proceeding, subject to very limited exceptions.

Further, prior to the completion of this offering, we expect to enter into indemnification agreements with each of our directors and executive officers that may be broader than the specific indemnification provisions contained under British Virgin Islands law. These indemnification agreements will require us, among other things, to indemnify our directors and executive officers against liabilities that may arise by reason of their status or service. These indemnification agreements will also require us to advance all expenses incurred by the directors and executive officers in investigating or defending any such action, suit, or proceeding. We believe that these agreements are necessary to attract and retain qualified individuals to serve as directors and executive officers.

The limitation of liability and indemnification provisions that are included in our amended memorandum and articles of association and in indemnification agreements that we enter into with our directors and executive officers may discourage shareholders from bringing a lawsuit against our directors and executive officers for breach of their fiduciary duties. They may also reduce the likelihood of derivative litigation against our directors and executive officers, even though an action, if successful, might benefit us and other shareholders. Further, a shareholder's investment may be harmed to the extent that we pay the costs of settlement and damage awards against directors and executive officers as required by these indemnification provisions. At present, we are not aware of any pending litigation or proceeding involving any person who is or was one of our directors, officers, employees or other agents or is or was serving at our request as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, for which indemnification is sought, and we are not aware of any threatened litigation that may result in claims for indemnification.

We have obtained insurance policies under which, subject to the limitations of the policies, coverage is provided to our directors and executive officers against loss arising from claims made by reason of breach of fiduciary duty or other wrongful acts as a director or executive officer, including claims relating to public securities matters, and to us with respect to payments that may be made by us to these directors and executive officers pursuant to our indemnification obligations or otherwise as a matter of law.

Certain of our non-employee directors may, through their relationships with their employers, be insured and/or indemnified against certain liabilities incurred in their capacity as members of our board of directors. The underwriting agreement provides for indemnification by the underwriters of us and our officers, directors and employees for certain liabilities arising under the Securities Act, or otherwise.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling our company pursuant to the foregoing provisions, we have been informed that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

#### **Rule 10b5-1 Sales Plans**

Our directors and executive officers may adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell common shares on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from them. The director or officer may amend a Rule 10b5-1 plan in some circumstances and may terminate a plan at any time. Our directors and executive officers also may buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material nonpublic information subject to compliance with the terms of our insider trading policy. Prior to 180 days after the date of this offering, subject to early termination, the sale of any shares under such plan would be prohibited by the lock-up agreement that the director or officer has entered into with the underwriters.

# CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

The following is a description of transactions since January 1, 2014 to which we have been a participant in which the amount involved exceeded or will exceed \$120,000, and in which any of our directors, executive officers or holders of more than 5% of our share capital, or any members of their immediate family, had or will have a direct or indirect material interest, other than compensation arrangements which are described under "Executive Compensation."

## **Participation in this Offering**

Certain of our existing principal shareholders, directors and their affiliated entities have agreed to purchase an aggregate of 3,142,117 common shares in this offering at the initial public offering price per share.

Furthermore, at our request, the underwriters have reserved for sale at the initial public offering price up to 495,000 common shares, or 5% of the common shares offered by this prospectus, for our employees, directors and other persons associated with us. If purchased by these persons, these shares will not be subject to a lock-up restriction, except in the case of shares purchased by any director or officer, which will be subject to the lock-up restrictions described in the "Underwriting" section of this prospectus.

#### **Relationship with Yale University**

In 2013, we entered into a license agreement with, and issued common shares to, Yale University, pursuant to which Yale became a holder of more than 5% of our outstanding voting securities. During the years ended December 31, 2014, 2015 and 2016, we made payments to Yale of \$24,000, \$84,000 and \$4,000, respectively, under the Yale license agreement. Yale ceased to be a holder of 5% of our outstanding shares as of December 31, 2014.

Dr. Coric, our Chief Executive Officer, is 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 we license from Yale. Under Yale's policies, as a co-inventor Dr. Coric is entitled to receive a share of any royalties that we pay to Yale under the agreement with respect to the covered intellectual property. No royalty payments have been made to date.

#### **Loan Guaranty Warrants**

In connection with our credit agreement with Wells Fargo entered into in August 2016, Wells Fargo required that we obtain a personal guaranty of our loan obligations from one of our directors, Mr. Childs. Another one of our directors, Dr. Bailey, provided a further guaranty related to the credit agreement. In exchange for their guaranties, in January 2017, we issued a warrant to each director to purchase 107,500 common shares at an exercise price of \$9.2911 per share. At the time of our entering into the credit agreement, Mr. Childs was also the beneficial owner of more than 5% of our outstanding common shares.

# **Transactions with Portage Biotech, Inc.**

In January 2014, we sold and issued 5,752,000 common shares to Portage Biotech, Inc., or Portage, at a purchase price of \$0.61 per share for gross proceeds of \$3.5 million. As a result of this transaction, Portage became a beneficial owner of more than 5% of our outstanding shares. In July 2015, we sold and issued 446,500 common shares to Portage at a purchase price of \$5.60 per share for gross proceeds of \$2.5 million. In February 2016, we sold and issued 143,000 common shares to Portage at a purchase price of \$7.00 per share for gross proceeds of \$1.0 million. Declan Doogan, the chairman of our board of directors, is the chief executive officer of Portage. Kamlesh Shah, one of our former directors who resigned in February 2017, is the chief financial officer of Portage.

### **Purchases of Common Shares By Directors**

In July 2015, Mr. Childs, one of our directors and a beneficial owner of more than 5% of our common shares, purchased 268,000 common shares at a purchase price of \$5.60 per share for gross proceeds to us of \$1.5 million. In February 2016, Mr. Childs purchased 286,000 common shares at a purchase price of \$7.00 per share for gross proceeds to us of \$2.0 million. In May 2016, Mr. Childs purchased 714,500 common shares at a purchase price of \$7.70 per share for gross proceeds to us of \$5.5 million.

In May 2016, Dr. Bailey, one of our directors, purchased 39,000 common shares at a purchase price of \$7.70 per share for gross proceeds to us of \$0.3 million.

# Transactions with Biohaven Pharmaceuticals, Inc.

In January 2014, we entered into a Master Services Agreement, or MSA, with Biohaven Pharmaceuticals, Inc., or BPI, pursuant to which we engaged BPI as our clinical research organization, or CRO, to perform services on our behalf, including conducting clinical trials, performing scientific research and assisting with the preparation of regulatory filings. The MSA was amended and restated in June 2014. From January 2014 until December 31, 2016, the sole beneficial stockholders of BPI were Dr. Coric, our Chief Executive Officer; Dr. Berman, our Chief Medical Officer; and Dr. Doogan, the chairman of our board of directors.

During the years ended December 31, 2014, 2015 and 2016, we made payments to BPI under the MSA in the amount of \$1.2 million, \$2.8 million and \$13.3 million, respectively. The vast majority of these amounts funded the operations of BPI, including the costs of third-party service providers.

On December 31, 2016, we entered into stock purchase agreements with each of the stockholders of BPI under which we acquired all of the outstanding capital stock of BPI for an aggregate purchase price of \$0.6 million. We paid the purchase price by the issuance of a promissory note to each stockholder of BPI in the principal amount of \$0.2 million. The notes, which bear interest at a fixed rate of 4.5% per year, are payable in five annual installments, the first four of which are interest only, with the final payment due on December 31, 2021 to include the principal balance outstanding and all accrued but unpaid interest, and are mandatorily payable upon the consummation of this offering.

In addition, the stock purchase agreements require us to indemnify and hold harmless (on an after-tax basis) each of the selling stockholders of BPI from and against, among other things, all federal, state and local income, self-employment, withholding and other similar taxes, plus any related liabilities, interest, penalties, losses, damages, costs, expenses (including fees for legal or accounting services) (whether or not such claim for taxes by a taxing authority is ultimately successful), other than U.S. federal capital gains taxes and state and local income taxes on the purchase price received by the selling stockholder and any U.S. federal, state and local income taxes on the promissory notes delivered to the selling stockholders of BPI in payment of the purchase price.

# **Sales of Series A Preferred Shares**

In October 2016 and February 2017, we sold an aggregate of 8,610,391 of our Series A preferred shares at a price of \$9.2911 per share for an aggregate purchase price of \$80.0 million, 2,113,313 shares of

which were sold to directors, executive officers and entities affiliated with our directors. The table below summarizes these sales.

Purchaser	Series A Preferred Shares Purchased	Aggregate Purchase Price
John W. Childs 2013 Revocable Trust	1,035,938	\$ 9,625,004
Gregory H. Bailey, M.D.	1,076,299	10,000,002
James Engelhart	1,076	9,997
Total	2,113,313	\$ 19,635,003

#### **Investor Rights Agreement and Shareholders' Agreement**

In connection with our Series A preferred share financing described above, we entered into an investor rights agreement and an amended and restated shareholders' agreement with the holders of preferred shares, including each of the persons and entities listed in the table above, as well as certain of our officers, directors and holders of 5% of our shares.

The investors' rights agreement, among other things:

- grants our preferred shareholders specified registration rights with respect to our common shares, including common shares issued or issuable upon conversion of the convertible preferred shares held by them; and
- obligates us to deliver periodic financial statements to some of the shareholders who are parties to the investor rights agreement.

For more information regarding the registration rights provided in this agreement, please refer to the section titled "Description of Share Capital—Registration Rights." The provisions of this agreement other than those relating to registration rights will terminate upon the closing of this offering.

The shareholders' agreement, among other things:

- provides for the voting of shares with respect to the constituency of our board of directors and the voting of shares in favor of specified transactions approved by our board of directors and the requisite majority of our shareholders;
- grants our shareholders a right of first refusal with respect to sales of our shares by us, subject to specified exclusions, which exclusions include the sale of the shares in this offering; and
- grants our shareholders rights of first refusal and tag-along rights with respect to proposed transfers of our securities by other shareholders.

The shareholders' agreement will terminate upon the closing of this offering.

#### **Indemnification Agreements**

Our amended and restated memorandum and articles of association will contain provisions limiting the liability of directors and providing that we will indemnify each of our directors to the fullest extent permitted under the BVI Companies Act. Our amended and restated memorandum and articles of association will also provide our board of directors with discretion to indemnify our officers and employees when determined appropriate by the board.

In addition, we intend to enter into indemnification agreements with each of our directors and executive officers prior to the completion of this offering. For more information regarding these agreements, see "Executive Compensation—Limitations on Liability and Indemnification Matters."

### **Related Person Transaction Policy**

Prior to this offering, we have not had a formal policy regarding approval of transactions with related parties. We have adopted a related person transaction policy that sets forth our procedures for the identification, review, consideration and approval or ratification of related person transactions. The policy became effective upon the execution of the underwriting agreement for this offering. For purposes of our policy only, a related person transaction is a transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we and any related person are, were or will be participants in which the amount involved exceeds \$120,000. Transactions involving compensation for services provided to us as an employee or director are not covered by this policy. A related person is any executive officer, director or beneficial owner of more than 5% of any class of our voting securities, including any of their immediate family members and any entity owned or controlled by such persons.

Under the policy, if a transaction has been identified as a related person transaction, including any transaction that was not a related person transaction when originally consummated or any transaction that was not initially identified as a related person transaction prior to consummation, our management must present information regarding the related person transaction to our audit committee, or, if audit committee approval would be inappropriate, to another independent body of our board of directors, for review, consideration and approval or ratification. The presentation must include a description of, among other things, the material facts, the interests, direct and indirect, of the related persons, the benefits to us of the transaction and whether the transaction is on terms that are comparable to the terms available to or from, as the case may be, an unrelated third party or to or from employees generally. Under the policy, we will collect information that we deem reasonably necessary from each director, executive officer and, to the extent feasible, significant shareholder to enable us to identify any existing or potential related-person transactions and to effectuate the terms of the policy. In addition, under our Code of Business Conduct and Ethics, which we have adopted and which will become effective as of the completion of this offering, our employees and directors will have an affirmative responsibility to disclose any transaction or relationship that reasonably could be expected to give rise to a conflict of interest. In considering related person transactions, our audit committee, or other independent body of our board of directors, will take into account the relevant available facts and circumstances including, but not limited to:

- the risks, costs and benefits to us;
- the impact on a director's independence in the event that the related person is a director, immediate family member of a director or an entity with which a director is affiliated;
- the availability of other sources for comparable services or products; and
- the terms available to or from, as the case may be, unrelated third parties or to or from employees generally.

The policy requires that, in determining whether to approve, ratify or reject a related person transaction, our audit committee, or other independent body of our board of directors, must consider, in light of known circumstances, whether the transaction is in, or is not inconsistent with, our best interests and those of our shareholders, as our audit committee, or other independent body of our board of directors, determines in the good faith exercise of its discretion.

# PRINCIPAL SHAREHOLDERS

The following table sets forth the beneficial ownership of our common shares as of February 28, 2017 for:

- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common shares;
- each of our named executive officers;
- each of our directors; and
- all of our current executive officers and directors as a group.

The percentage ownership information shown in the column titled "Before Offering" in the table is based upon 22,447,060 common shares outstanding as of February 28, 2017, after giving effect to the conversion of all of our Series A preferred shares into 9,358,560 common shares, which will occur automatically upon the closing of this offering. The percentage ownership information shown in the column titled "After Offering" in the table is based on 34,230,583 common shares outstanding after this offering, assuming 9,900,000 common shares being sold in the offering and after giving effect to the issuance of an aggregate of 1,883,523 common shares to BMS and AstraZeneca in connection with the offering.

We have determined beneficial ownership in accordance with the rules of the SEC. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities. In addition, the rules include common shares issuable pursuant to the exercise of stock options or warrants that are exercisable on or before April 29, 2017, which is 60 days after February 28, 2017. These shares are deemed to be outstanding and beneficially owned by the person holding those options or warrants for the purpose of computing the percentage ownership of that person, but they are not treated as outstanding for the purpose of computing the percentage ownership of any other person.

Certain of our existing principal shareholders, directors and their affiliated entities have agreed to purchase an aggregate of 3,142,117 common shares in this offering at the initial public offering price per share. The following table does not reflect such purchases by these entities in this offering, nor does it give effect to any shares that may be acquired by our shareholders, directors or executive officers pursuant to the directed share program.

Unless otherwise indicated, the persons or entities identified in this table have sole voting and investment power with respect to all shares shown as beneficially owned by them, subject to applicable community property laws.

Except as otherwise noted below, the address for persons listed in the table is c/o Biohaven Pharmaceutical Holding Company Ltd., 234 Church Street, New Haven, CT 06510.

	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned	
Name of Beneficial Owner		Before Offering	After Offering
Principal Shareholders:			
Portage Biotech, Inc. <sup>(1)</sup>	6,341,500	28.3%	18.5%
Vivo Capital Fund VIII, L.P. <sup>(2)</sup>	1,506,818	6.7	4.4
RA Capital Healthcare Fund, L.P. <sup>(3)</sup>	1,143,137	5.1	3.3
Executive Officers and Directors:			
Vlad Coric, M.D. <sup>(4)</sup>	1,587,500	7.0	4.6
Robert Berman, M.D. <sup>(5)</sup>	1,550,500	6.8	4.5
James Engelhart <sup>(6)</sup>	97,955	*	*
John Tilton <sup>(7)</sup>	34,948	*	*
Charles Conway, Ph.D. <sup>(7)</sup>	13,500	*	*
Kimberly Gentile <sup>(7)</sup>	65,250	*	*
Declan Doogan, M.D. <sup>(8)</sup>	1,587,500	7.0	4.6
Gregory H. Bailey, M.D. <sup>(9)</sup>	1,466,599	6.4	4.2
John W. Childs <sup>(10)</sup>	2,655,738	11.6	7.7
Albert Cha, M.D., Ph.D. <sup>(2)(11)</sup>	1,514,318	6.7	4.4
Eric Aguiar, M.D. <sup>(7)</sup>	7,500	*	*
All current directors and executive officers as a group (11 persons) <sup>(12)</sup>	10,581,308	43.7	29.4

<sup>\*</sup> Represents beneficial ownership of less than 1%.

- Consists of 6,341,500 common shares. Portage Biotech, Inc. is a publicly-traded company listed on the Canadian Securities Exchange (PBT.U). The principal business address of Portage Biotech, Inc. is c/o Portage Services Ltd., 47 Avenue Road., Suite 200, Toronto, ON M5R 2G3 Canada.
- (2) Consists of (a) 1,323,990 common shares issuable upon conversion of Series A preferred shares held by Vivo Capital Fund VIII, L.P. and (b) 182,828 common shares issuable upon conversion of Series A preferred shares held by Vivo Capital Surplus Fund VIII, L.P. Vivo Capital VIII LLC is the general partner of both Vivo Capital Fund VIII L.P. and Vivo Capital Surplus Fund VIII L.P. The voting members of Vivo Capital VIII, LLC are Frank Kung, Albert Cha, Edgar Engleman, Chen Yu and Shan Fu, none of whom has individual voting or investment power with respect to these shares and each of whom disclaims beneficial ownership of such shares. The principal business address of Vivo Capital is 505 Hamilton Avenue, Suite 207, Palo Alto, CA 94301.
- (3) Consists of 1,143,137 common shares issuable upon conversion of Series A preferred shares. RA Capital Healthcare Fund, L.P., whose general partner is RA Capital Management, LLC and Peter Kolchinsky is Managing Member of RA Capital Management, LLC. Shared voting or investment power is held by RA Capital Management, LLC, as the General Partner of RA Capital Healthcare Fund, L.P., and Mr. Kolchinsky as Managing Member of RA Capital Management, LLC. The address for RA Capital Healthcare Fund, L.P. is 20 Park Plaza, Ste. 1200, Boston, MA 02116.
- (4) Consists of (a) 287,500 common shares underlying options that are vested and exercisable within 60 days of February 28, 2017, (b) 650,000 common shares held by The Vladimir Coric Family Trust 2013 and (c) 650,000 common shares held by The Vladimir Coric Marital Trust 2013.

- (5) Consists of (a) 250,500 common shares underlying options that are vested and exercisable within 60 days of February 28, 2017, (b) 650,000 common shares held by The Berman Family Trust 2013 and (c) 650,000 common shares held by The Berman Marital Trust 2013.
- (6) Consists of (a) 1,076 common shares issuable upon conversion of Series A preferred shares and (b) 96,879 common shares underlying options that are vested and exercisable within 60 days of February 28, 2017.
- (7) Consists of common shares underlying options that are vested and exercisable within 60 days of February 28, 2017.
- (8) Consists of (a) 1,300,000 common shares held by the Declan Doogan 2014 Trust and (b) 287,500 common shares underlying options that are vested and exercisable within 60 days of February 28, 2017.
- (9) Consists of (a) 39,000 common shares, (b) 1,076,299 common shares issuable upon conversion of Series A preferred shares, (c) 243,800 common shares underlying options that are vested and exercisable within 60 days of February 28, 2017 and (d) 107,500 common shares underlying immediately exercisable warrants. 538,150 of the Series A preferred shares are pledged as collateral by Dr. Bailey to John Childs, another director, to secure Dr. Bailey's obligation to reimburse Mr. Childs for one-half of any guaranty obligations that Mr. Childs pays to Wells Fargo pursuant to Mr. Childs' guaranty of our credit agreement with Wells Fargo. This pledge will terminate upon our repayment of outstanding borrowings under the credit agreement, which we expect will occur upon completion of this offering.
- (10) Consists of (a) 1,268,500 common shares, (b) 1,035,938 common shares issuable upon conversion of Series A preferred shares held by the John W. Childs 2013 Revocable Trust, (c) 243,800 common shares underlying options that are vested and exercisable within 60 days of February 28, 2017 and (d) 107,500 common shares underlying immediately exercisable warrants.
- (11) Includes 7,500 common shares underlying options that are vested and exercisable within 60 days of February 28, 2017.
- (12) Consists of (a) 5,207,500 common shares, (b) 3,620,131 common shares issuable upon conversion of Series A preferred shares, (c) 1,538,677 common shares underlying options that are vested and exercisable within 60 days of February 28, 2017 and (d) 215,000 common shares underlying immediately exercisable warrants.

# **DESCRIPTION OF SHARE CAPITAL**

The following descriptions are summaries of the material terms of our amended memorandum and articles of association to be in effect following the closing of this offering. Reference is made to the more detailed provisions of, and the descriptions are qualified in their entirety by reference to, the memorandum and articles of association. Please note that this summary is not intended to be exhaustive. For further information, please refer to the full version of our memorandum and articles of association which is included as an exhibit to the registration statement of which this prospectus is part.

#### General

We are a company incorporated in the British Virgin Islands on September 25, 2013, and our affairs are governed by the provisions of our memorandum of association and articles of association, as amended and restated from time to time, and by the provisions of applicable British Virgin Islands law.

#### **Authorized Share Capital**

Upon the completion of this offering, our amended and restated memorandum and articles of association will authorize us to issue up to 200,000,000 common shares, no par value, and 10,000,000 preferred shares, no par value, all of which preferred shares will be undesignated. Our board of directors may establish the rights and preferences of the preferred shares from time to time. As of February 28, 2017, after giving effect to the conversion of all outstanding preferred shares into common shares, there would have been 22,447,060 common shares issued and outstanding, held of record by 61 shareholders.

#### **Common Shares**

Holders of common shares are entitled to cast one vote for each share on all matters submitted to a vote of shareholders, including the election of directors.

Holders of common shares are entitled to receive ratably such dividends, if any, as may be declared by the board of directors out of funds legally available therefor, subject to the preferential rights in respect of any preferred shares. See "Dividend Policy." Holders of common shares do not have any preemptive or other rights to subscribe for additional shares pursuant to our memorandum and articles of association.

All holders of common shares are entitled to share ratably in any assets for distribution to shareholders upon the liquidation, dissolution or winding up of the company, subject to the preferential rights in respect of any preferred shares.

The memorandum and articles of association permit the board of directors to authorize the redemption, purchase or other acquisition of the common shares. All outstanding common shares are fully paid and nonassessable.

Holders of common shares have no conversion or subscription rights and there are no redemption or sinking fund provisions applicable to the common shares. The rights, preferences and privileges of the holders of common shares are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred shares that we may designate in the future.

#### **Preferred Shares**

Following the completion of this offering, our board of directors will have the authority, without further action by our shareholders, to issue up to 10,000,000 preferred shares in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon, and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

Our board of directors may authorize the issuance of preferred shares with voting or conversion rights that could adversely affect the voting power or other rights of the holders of our common shares. The purpose of authorizing our board of directors to issue preferred shares and determine its rights and preferences is to eliminate delays associated with a shareholder vote on specific issuances. The issuance of preferred shares, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in control of us and may adversely affect the market price of our common shares and the voting and other rights of the holders of our common shares. It is not possible to state the actual effect of the issuance of any preferred shares on the rights of holders of common shares until the board of directors determines the specific rights attached to the preferred shares.

# **Options**

Our 2014 Equity Incentive Plan, as amended, or the 2014 Plan, provides for us 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. As of December 31, 2016, options to purchase 3,864,425 common shares were outstanding. For additional information regarding the terms of the 2014 Plan, see "Executive Compensation—Equity Incentive Plans."

#### Warrants

On August 10, 2015, as partial consideration in connection with a license agreement, we issued a warrant to ALS Biopharma LLC, or ALS Biopharma, to purchase 275,000 common shares at an exercise price of \$5.60 per share. The warrant was immediately exercisable upon issuance and is exercisable for a period of 10 years from the issuance date.

On August 10, 2015, as partial consideration in connection with a license agreement, we issued a warrant to ALS Biopharma to purchase 325,000 common shares at an exercise price of \$5.60 per share. The warrant became exercisable in May 2016 upon the achievement of a specified regulatory milestone and is exercisable for a period of 10 years from the issuance date.

In connection with our credit agreement with Wells Fargo, we issued warrants to two of our directors, John Childs and Gregory Bailey, to purchase 107,500 common shares each, at an exercise price of \$9.2911 per share. The warrants were immediately exercisable upon issuance and may be exercised from the issuance date through the earlier of (i) the fifth anniversary of the issuance date or (ii) the second anniversary of our initial public offering.

### **Registration Rights**

We and the holders of our existing convertible preferred shares and certain holders of our common shares have entered into an amended and restated investors' rights agreement. The registration rights provisions of this agreement provide those holders with demand, piggyback and Form S-3 registration rights with respect to the common shares currently held by them, acquired by them in the future and issuable to them upon conversion of our convertible preferred shares.

# **Demand Registration Rights**

At any time beginning October 28, 2021, the holders of at least 50% of the registrable securities then outstanding have the right to demand that we file a registration statement on Form S-1 with respect to at least 40% of the registrable securities then outstanding, or a less percent if the anticipated offering price, net of selling expenses, would exceed \$10.0 million. These registration rights are subject to specified conditions and limitations, including the right of the underwriters, if any, to limit the number of shares included in any such registration under specified circumstances. Upon such a request, we are required to effect the registration as soon as practicable, but in any event no later than 60 days after the receipt of such

request. Because the investor rights agreement terminates on the third anniversary of this offering, no common shares will be entitled to these demand registration rights.

## **Piggyback Registration Rights**

If we propose to register any of our securities under the Securities Act either for our own account or for the account of other stockholders, the holders of registrable securities will each be entitled to notice of the registration and will be entitled to include their common shares in the registration statement. These piggyback registration rights are subject to specified conditions and limitations, including the right of the underwriters to limit the number of shares included in any such registration under specified circumstances. Approximately 23,000,000 common shares will be entitled to these piggyback registration rights.

### **Registration on Form S-3**

At any time after we become eligible to file a registration statement on Form S-3, the holders of at least 10% of the registrable securities then outstanding will each be entitled, upon any such holders' written request, to have such shares registered by us on a Form S-3 registration statement at our expense. These Form S-3 registration rights are subject to other specified conditions and limitations, including the condition that the anticipated aggregate offering price, net of selling expenses, exceeds \$5.0 million. Upon receipt of this request, the holders of all registrable securities then outstanding will each be entitled to participate in this registration, and we will be required to effect the registration within 45 days after the receipt of such request from the initiating holders. Approximately 11,000,000 common shares will be entitled to these S-3 registration rights.

#### **Expenses of Registration**

We will pay all expenses relating to any demand, piggyback or Form S-3 registration, other than underwriting discounts and commissions, subject to specified conditions and limitations.

#### **Termination of Registration Rights**

The registration rights granted under the investors' rights agreement will terminate upon the earlier of the third anniversary of the closing of this offering, the closing of a deemed liquidation event as defined in our memorandum and article of association or at such time as Rule 144 or another similar exemption under the Securities Act is available for the sale of all such holders of registrable securities' shares without limitation during a three-month period without registration.

# Limitations on the Right to Own Shares

There are no limitations on the right to own our common shares.

### **Disclosure of Shareholder Ownership**

There are no provisions in the memorandum and articles of association governing the ownership threshold above which shareholder ownership must be disclosed.

#### **Differences in Corporate Law**

The BVI Business Companies Act, or the BVI Act, and the laws of the British Virgin Islands, or the BVI, affecting BVI business companies like us and our shareholders differ from laws applicable to U.S. corporations and their shareholders. Set forth below is a summary of the significant differences between the provisions of the laws of the BVI applicable to us and the laws applicable to companies incorporated in the United States and their shareholders.

### Mergers and Similar Arrangements

Under the laws of the BVI, two or more companies may merge or consolidate in accordance with Section 170 of the BVI Act. A merger means the merging of two or more constituent companies into one of the constituent companies and a consolidation means the uniting of two or more constituent companies into a new company. In order to merge or consolidate, the directors of each constituent company must approve a written plan of merger or consolidation, which must be authorized by a resolution of shareholders.

While a director may vote on the plan of merger or consolidation even if he has a financial interest in the plan, the interested director must disclose the interest to all other directors of the company promptly upon becoming aware of the fact that he is interested in a transaction entered into or to be entered into by the company.

A transaction entered into by our company in respect of which a director is interested (including a merger or consolidation) is voidable by us unless the director's interest was (a) disclosed to the board prior to the transaction or (b) the transaction is (i) between the director and the company and (ii) the transaction is in the ordinary course of the company's business and on usual terms and conditions.

Notwithstanding the above, a transaction entered into by the company is not voidable if the material facts of the interest are known to the shareholders and they approve or ratify it or the company received fair value for the transaction.

Shareholders not otherwise entitled to vote on the merger or consolidation may still acquire the right to vote if the plan of merger or consolidation contains any provision which, if proposed as an amendment to the M&A, would entitle them to vote as a class or series on the proposed amendment. In any event, all shareholders must be given a copy of the plan of merger or consolidation irrespective of whether they are entitled to vote at the meeting to approve the plan of merger or consolidation.

The shareholders of the constituent companies are not required to receive shares of the surviving or consolidated company but may receive debt obligations or other securities of the surviving or consolidated company, other assets, or a combination thereof. Further, some or all of the shares of a class or series may be converted into a kind of asset while the other shares of the same class or series may receive a different kind of asset. As such, not all the shares of a class or series must receive the same kind of consideration.

After the plan of merger or consolidation has been approved by the directors and authorized by a resolution of the shareholders, articles of merger or consolidation are executed by each company and filed with the Registrar of Corporate Affairs in the BVI.

A shareholder may dissent from a mandatory redemption of his shares, an arrangement (if permitted by the court), a merger (unless the shareholder was a shareholder of the surviving company prior to the merger and continues to hold the same or similar shares after the merger) or a consolidation. A shareholder properly exercising his dissent rights is entitled to a cash payment equal to the fair value of his shares.

A shareholder dissenting from a merger or consolidation must object in writing to the merger or consolidation before the vote by the shareholders on the merger or consolidation, unless notice of the meeting was not given to the shareholder. If the merger or consolidation is approved by the shareholders, the company must give notice of this fact to each shareholder within 20 days who gave written objection. These shareholders then have 20 days to give to the company their written election in the form specified by the BVI Act to dissent from the merger or consolidation, provided that in the case of a merger, the 20 days starts when the plan of merger is delivered to the shareholder.

Upon giving notice of his election to dissent, a shareholder ceases to have any shareholder rights except the right to be paid the fair value of his shares. As such, the merger or consolidation may proceed in the ordinary course notwithstanding his dissent.

Within seven days of the later of the delivery of the notice of election to dissent and the effective date of the merger or consolidation, the company must make a written offer to each dissenting shareholder to purchase his shares at a specified price per share that the company determines to be the fair value of the shares. The company and the shareholder then have 30 days to agree upon the price. If the company and a shareholder fail to agree on the price within the 30 days, then the company and the shareholder shall, within 20 days immediately following the expiration of the 30-day period, each designate an appraiser and these two appraisers shall designate a third appraiser. These three appraisers shall fix the fair value of the shares as of the close of business on the day prior to the shareholders' approval of the transaction without taking into account any change in value as a result of the transaction.

### Shareholders' Suits

There are both statutory and common law remedies available to our shareholders as a matter of BVI law. These are summarized below:

### Prejudiced Members

A shareholder who considers that the affairs of the company have been, are being, or are 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, can apply to the court under Section 184I of the BVI Act, among other things, for an order that his shares be acquired, that he be provided compensation, that the Court regulate the future conduct of the company, or that any decision of the company which contravenes the BVI Act or our memorandum and articles of association be set aside.

#### **Derivative** Actions

Section 184C of the BVI Act provides that a shareholder of a company may, with the leave of the Court, bring an action in the name of the company to redress any wrong done to it.

### Just and Equitable Winding Up

In addition to the statutory remedies outlined above, shareholders can also petition for the winding up of a company on the grounds that it is just and equitable for the court to so order. Save in exceptional circumstances, this remedy is only available where the company has been operated as a quasi partnership and trust and confidence between the partners has broken down.

#### Indemnification of Directors and Executive Officers and Limitation of Liability

Under our M&A, we indemnify against all expenses, including legal fees, and against all judgments, fines and amounts paid in settlement and reasonably incurred in connection with legal, administrative or investigative proceedings for any person who:

- is or was a party or is threatened to be made a party to any threatened, pending or completed proceedings, whether civil, criminal, administrative or investigative, by reason of the fact that the person is or was our director; or
- is or was, at our request, serving as a director or officer of, or in any other capacity is or was acting for, another body corporate or a partnership, joint venture, trust or other enterprise.

These indemnities only apply if the person acted honestly and in good faith with a view to our best interests and, in the case of criminal proceedings, the person had no reasonable cause to believe that his conduct was unlawful. This standard of conduct is generally the same as permitted under the Delaware General Corporation Law for a Delaware corporation.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to our directors, officers or persons controlling us under the foregoing provisions, we have been advised that in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

#### Anti-takeover Provisions in Our Memorandum and Articles of Association

Some provisions of our M&A may discourage, delay or prevent a change in control of our company or management that shareholders may consider favorable. Yet, under BVI law, our directors may only exercise the rights and powers granted to them under our M&A, as they believe in good faith to be in the best interests of our company.

### **Directors' Fiduciary Duties**

Under Delaware corporate law, a director of a Delaware corporation has a fiduciary duty to the corporation and its shareholders. This duty has two components: the duty of care and the duty of loyalty. The duty of care requires that a director act in good faith, with the care that an ordinarily prudent person would exercise under similar circumstances. Under this duty, a director must inform himself of, and disclose to shareholders, all material information reasonably available regarding a significant transaction. The duty of loyalty requires that a director act in a manner he reasonably believes to be in the best interests of the corporation. He must not use his corporate position for personal gain or advantage. This duty prohibits self-dealing by a director and mandates that the best interest of the corporation and its shareholders take precedence over any interest possessed by a director, officer or controlling shareholder and not shared by the shareholders generally. In general, actions of a director are presumed to have been made on an informed basis, in good faith and in the honest belief that the action taken was in the best interests of the corporation. However, this presumption may be rebutted by evidence of a breach of one of the fiduciary duties. Should such evidence be presented concerning a transaction by a director, a director must prove the procedural fairness of the transaction and that the transaction was of fair value to the corporation.

Under BVI law, our directors owe the company certain statutory and fiduciary duties including, among others, a duty to act honestly, in good faith, for a proper purpose and with a view to what the directors believe to be in the best interests of the company. Our directors are also required, when exercising powers or performing duties as a director, to exercise the care, diligence and skill that a reasonable director would exercise in comparable circumstances, taking into account without limitation, the nature of the company, the nature of the decision and the position of the director and the nature of the responsibilities undertaken. In the exercise of their powers, our directors must ensure neither they nor the company acts in a manner which contravenes the BVI Act or our M&A. A shareholder has the right to seek damages for breaches of duties owed to us by our directors.

### Shareholder Action by Written Consent

Under the Delaware General Corporation Law, a corporation may eliminate the right of shareholders to act by written consent by amendment to its certificate of incorporation. BVI law provides that shareholders may approve corporate matters by way of a written resolution without a meeting signed by or on behalf of shareholders sufficient to constitute the requisite majority of shareholders who would have been entitled to vote on such matter at a general meeting; provided that if the consent is less than unanimous, notice must be given to all non-consenting shareholders.

#### Shareholder Proposals

Under the Delaware General Corporation Law, a shareholder has the right to put any proposal before the annual meeting of shareholders, provided it complies with the notice provisions in the governing

documents. A special meeting may be called by the board of directors or any other person authorized to do so in the governing documents, but shareholders may be precluded from calling special meetings. Our memorandum and articles of association allow our shareholders holding not less than 10% of the votes of the outstanding voting shares to requisition a shareholders' meeting. We are not obliged by law to call shareholders' annual general meetings, but our memorandum and articles of association do permit the directors to call such a meeting and we intend to hold annual meetings of shareholders following the completion of this offering. The location of any shareholders' meeting can be determined by the board of directors and can be held anywhere in the world.

#### **Cumulative Voting**

Under the Delaware General Corporation Law, cumulative voting for elections of directors is not permitted unless the corporation's certificate of incorporation specifically provides for it. Cumulative voting potentially facilitates the representation of minority shareholders on a board of directors since it permits the minority shareholder to cast all the votes to which the shareholder is entitled on a single director, which increases the shareholder's voting power with respect to electing such director. As permitted under BVI law, our memorandum and articles of association do not provide for cumulative voting. As a result, our shareholders are not afforded any less protections or rights on this issue than shareholders of a Delaware corporation.

#### **Removal of Directors**

Under the Delaware General Corporation Law, a director of a corporation with a classified board may be removed only for cause with the approval of a majority of the outstanding shares entitled to vote, unless the certificate of incorporation provides otherwise. Under our memorandum and articles of association, directors can be removed from office, with cause, by a resolution of shareholders passed at a meeting called for the purpose of removing the director or for purposes including the removal of the director.

#### **Transactions with Interested Shareholders**

The Delaware General Corporation Law contains a business combination statute applicable to Delaware public corporations whereby, unless the corporation has specifically elected not to be governed by such statute by amendment to its certificate of incorporation, it is prohibited from engaging in certain business combinations with an "interested shareholder" for three years following the date that such person becomes an interested shareholder. An interested shareholder generally is a person or group who or which owns or owned 15% or more of the target's outstanding voting shares within the past three years. This has the effect of limiting the ability of a potential acquirer to make a two-tiered bid for the target in which all shareholders would not be treated equally. The statute does not apply if, among other things, prior to the date on which such shareholder becomes an interested shareholder. This encourages any potential acquirer of a Delaware public corporation to negotiate the terms of any acquisition transaction with the target's board of directors. BVI law has no comparable statute.

### Dissolution; Winding Up

Under the Delaware General Corporation Law, unless the board of directors approves the proposal to dissolve, dissolution must be approved by shareholders holding 100% of the total voting power of the corporation. Only if the dissolution is initiated by the board of directors may it be approved by a simple majority of the corporation's outstanding shares. Delaware law allows a Delaware corporation to include in its certificate of incorporation a supermajority voting requirement in connection with dissolutions initiated

by the board. Under the BVI Act and our memorandum and articles of association, we may appoint a voluntary liquidator by a resolution of the shareholders or by resolution of directors.

## Variation of Rights of Shares

Under the Delaware General Corporation Law, a corporation may vary the rights of a class of shares with the approval of a majority of the outstanding shares of such class, unless the certificate of incorporation provides otherwise.

#### **Amendment of Governing Documents**

Under the Delaware General Corporation Law, a corporation's governing documents may be amended with the approval of a majority of the outstanding shares entitled to vote, unless the certificate of incorporation provides otherwise. As permitted by BVI, our memorandum and articles of association may be amended by a resolution of shareholders and by a resolution of directors. Any amendment is effective from the date it is registered at the Registry of Corporate Affairs in the BVI.

# **Transfer Agent and Registrar**

The transfer agent and registrar for our common shares is American Stock Transfer & Trust Company, LLC. The transfer agent's address is 6201 15<sup>th</sup> Avenue, Brooklyn, NY 11219.

# **Stock Exchange Listing**

Our common shares have been approved for listing on the New York Stock Exchange under the trading symbol "BHVN."

### SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, no public market existed for our common shares. Future sales of our common shares in the public market after this offering, or the perception that these sales could occur, could adversely affect prevailing market prices for our common shares and could impair our future ability to raise equity capital.

Based on the number of shares outstanding as of February 28, 2017, upon completion of this offering and assuming no exercise of the underwriters' option to purchase additional shares, 34,230,583 common shares will be outstanding, assuming no outstanding options or warrants are exercised. For a description of the impact of changes in the offering price, see "Prospectus Summary—The Offering." All of the common shares sold in this offering will be freely tradable without restrictions or further registration under the Securities Act, except for any shares sold to our "affiliates," as that term is defined under Rule 144 under the Securities Act. The remaining common shares held by existing shareholders are "restricted securities," as that term is defined in Rule 144 under the Securities Act. Restricted securities may be sold in the public market only if registered or if their resale qualifies for exemption from registration described below under Rule 144 promulgated under the Securities Act.

As a result of contractual restrictions described below and the provisions of Rules 144 and 701, the shares sold in this offering and the restricted securities will be available for sale in the public market as follows:

- the 9,900,000 shares sold in this offering will be eligible for immediate sale upon the completion of this offering; and
- the 24,330,583 restricted shares outstanding prior to the completion of this offering will be eligible for sale in the public market upon expiration of lock-up agreements 180 days after the date of this prospectus, subject in certain circumstances to the volume, manner of sale and other limitations under Rule 144 and Rule 701.

Certain of our existing principal shareholders, directors and their affiliates have agreed to purchase an aggregate of 3,142,117 common shares in this offering at the initial public offering price per share. Such shares purchased by these entities cannot be resold in the public market immediately following this offering as a result of restrictions under securities laws and lock-up agreements, but will be able to be sold following the expiration of these restrictions, in each case as described below.

Any common shares sold to our directors or executive officers pursuant to the directed share program will be subject to the 180-day lock-up restrictions described in the "Underwriting" section of this prospectus.

#### **Rule 144**

In general, persons who have beneficially owned restricted common shares for at least six months, and any affiliate of the company who owns either restricted or unrestricted common shares, are entitled to sell their securities without registration with the SEC under an exemption from registration provided by Rule 144 under the Securities Act.

#### Non-Affiliates

Any person who is not deemed to have been one of our affiliates at the time of, or at any time during the three months preceding, a sale may sell an unlimited number of restricted securities under Rule 144 if:

the restricted securities have been held for at least six months, including the holding period of any prior owner other than one of our affiliates;

- we have been subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale; and
- we are current in our Exchange Act reporting at the time of sale.

Any person who is not deemed to have been an affiliate of ours at the time of, or at any time during the three months preceding, a sale and has held the restricted securities for at least one year, including the holding period of any prior owner other than one of our affiliates, will be entitled to sell an unlimited number of restricted securities without regard to the length of time we have been subject to Exchange Act periodic reporting or whether we are current in our Exchange Act reporting.

#### **Affiliates**

Persons seeking to sell restricted securities who are our affiliates at the time of, or any time during the three months preceding, a sale, would be subject to the restrictions described above. They are also subject to additional restrictions, by which such person would be required to comply with the manner of sale and notice provisions of Rule 144 and would be entitled to sell within any three-month period only that number of securities that does not exceed the greater of either of the following:

- 1% of the number of common shares then outstanding, which will equal approximately 342,000 shares immediately after the completion of this offering based on the number of shares outstanding as of February 28, 2017; or
- the average weekly trading volume of our common shares on the stock exchange on which our shares are listed during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale.

Additionally, persons who are our affiliates at the time of, or any time during the three months preceding, a sale may sell unrestricted securities under the requirements of Rule 144 described above, without regard to the six month holding period of Rule 144, which does not apply to sales of unrestricted securities.

# **Rule 701**

Rule 701 under the Securities Act, as in effect on the date of this prospectus, permits resales of shares in reliance upon Rule 144 but without compliance with certain restrictions of Rule 144, including the holding period requirement. Most of our employees, executive officers or directors who purchased shares under a written compensatory plan or contract may be entitled to rely on the resale provisions of Rule 701, but all holders of Rule 701 shares are required to wait until 90 days after the date of this prospectus before selling their shares. However, substantially all Rule 701 shares are subject to lock-up agreements as described below and in the section of this prospectus titled "Underwriting" and will become eligible for sale upon the expiration of the restrictions set forth in those agreements.

#### **Form S-8 Registration Statements**

As soon as practicable after the completion of this offering, we intend to file with the SEC one or more registration statements on Form S-8 under the Securities Act to register the common shares that are issuable pursuant to the 2014 Plan and the 2017 plan. These registration statements will become effective immediately upon filing. Shares covered by these registration statements will then be eligible for sale in the public markets, subject to vesting restrictions, any applicable lock-up agreements described below and Rule 144 limitations applicable to affiliates.

# **Lock-Up Agreements**

We and the holders of all of our common shares outstanding on the date of this prospectus, including each of our executive officers and directors, have entered into lock-up agreements with the underwriters or otherwise agreed, subject to certain exceptions, that we and they will not, directly or indirectly, offer, sell, contract to sell, pledge, grant any option to purchase, make any short sale, or otherwise dispose of or hedge any of our common shares, any options or warrants to purchase common shares, or any securities convertible into, or exchangeable for or that represent the right to receive common shares, without the prior written consent of the representatives of the underwriters for a period of 180 days from the date of this prospectus.

# MATERIAL UNITED STATES FEDERAL INCOME CONSIDERATIONS FOR U.S. HOLDERS

The following is a summary of material U.S. federal income tax considerations relating to the acquisition, ownership and disposition of our common shares by a U.S. holder (as defined below). This summary addresses only the U.S. federal income tax considerations for U.S. holders that are initial purchasers of our common shares pursuant to this offering and that will hold such common shares as capital assets for U.S. federal income tax purposes. This summary does not address all U.S. federal income tax matters that may be relevant to a particular U.S. holder. This summary does not address tax considerations applicable to a holder of our common shares that may be subject to special tax rules including, without limitation, the following:

- banks, financial institutions or insurance companies;
- brokers, dealers or traders in securities, currencies, commodities, or notional principal contracts;
- tax-exempt entities or organizations, including an "individual retirement account" or "Roth IRA" as defined in Section 408 or 408A of the Code, respectively;
- real estate investment trusts, regulated investment companies or grantor trusts;
- persons that hold the common shares as part of a "hedging," "integrated" or "conversion" transaction or as a position in a "straddle" for U.S. federal income tax purposes;
- partnerships (including entities classified as partnerships for U.S. federal income tax purposes) or other pass-through entities, or persons that will hold the common shares through such an entity;
- certain former citizens or long-term residents of the United States;
- holders that own directly, indirectly, or through attribution 10% or more of the voting power or value of our common shares;
- holders that have a "functional currency" for U.S. federal income tax purposes other than the U.S. dollar; and
- investors in this offering who are existing shareholders of our company.

Further, this summary does not address the U.S. federal estate, gift, or alternative minimum tax considerations, or any U.S. state, local, or non-U.S. tax considerations of the acquisition, ownership and disposition of our common shares.

This description is based on the Code; existing, proposed and temporary U.S. Treasury Regulations promulgated thereunder; and administrative and judicial interpretations thereof, in each case as in effect and available on the date hereof. All the foregoing is subject to change, which change could apply retroactively, and to differing interpretations, all of which could affect the tax considerations described below. There can be no assurances that the U.S. Internal Revenue Service, or the IRS, will not take a contrary or different position concerning the tax consequences of the acquisition, ownership and disposition of our common shares or that such a position would not be sustained. Holders are urged to consult their own tax advisers concerning the U.S. federal, state, local and non-U.S. tax consequences of acquiring, owning, and disposing of our common shares in their particular circumstances.

For the purposes of this summary, a "U.S. holder" is a beneficial owner of our common shares that is (or is treated as), for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity that is treated as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust, (a) if a court within the United States is able to exercise primary supervision over its administration and one or more U.S. persons have the authority to control all of the substantial

decisions of such trust or (b) that has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a U.S. person

If a partnership (or any other entity or arrangement treated as a partnership for U.S. federal income tax purposes) holds our common shares, the U.S. federal income tax consequences relating to an investment in the common shares will depend in part upon the status of the partner and the activities of the partnership. Such a partner or partnership is urged to consult its tax advisor regarding the U.S. federal income tax considerations of acquiring, owning and disposing of our common shares in its particular circumstances.

As indicated below, this discussion is subject to U.S. federal income tax rules applicable to a "passive foreign investment company," or a PFIC.

Persons considering an investment in our common shares are urged to consult their own tax advisors as to the particular tax consequences applicable to them relating to the acquisition, ownership and disposition of our common shares, including the applicability of U.S. federal, state and local tax laws and non-U.S. tax laws.

#### Tax Residence

Generally, for U.S. federal tax purposes, a corporation is 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 British Virgin Islands incorporated entity, we would be classified as a foreign corporation under these general rules. Section 7874 of the Code, or 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'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, 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 Biohaven Pharmaceuticals, Inc., a Delaware corporation, or 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 (see "Certain Relationships and Related Party Transactions—Transactions with Biohaven Pharmaceuticals, Inc."). 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 shares. 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. The remainder of this discussion assumes that we are properly classified as a foreign corporation for U.S. federal tax purposes.

# **Distributions**

Although we do not currently plan to pay dividends, and subject to the discussion under "Passive Foreign Investment Company Considerations," below, a U.S. Holder generally will be required to treat the

gross amount of any distribution actually or constructively received with respect to our common shares as a dividend to the extent of the U.S. holder's pro rata share of our current and accumulated earnings and profits as determined under U.S. federal income tax principles. Distributions in excess of earnings and profits generally will be non-taxable to the U.S. holder to the extent of, and will be applied against and reduce, the U.S. holder's adjusted tax basis in the common shares. Distributions in excess of earnings and profits and such adjusted tax basis will generally be taxable to the U.S. holder as either long-term or short-term capital gain depending upon whether the U.S. holder has held the common shares for more than one year as of the time such distribution is received. However, since we may not calculate our earnings and profits under U.S. federal income tax principles, a U.S. holder should assume that any distribution with respect to our common shares will constitute ordinary dividend income.

Non-corporate U.S. holders may qualify for the preferential rates of taxation with respect to dividends on our common shares applicable to long-term capital gains (i.e., gains from the sale of capital assets held for more than one year) applicable to qualified dividend income (as discussed below) if we are a "qualified foreign corporation" and certain other requirements (discussed below) are met. A non-U.S. corporation (other than a corporation that is classified as a PFIC for the taxable year in which the dividend is paid or the preceding taxable year) generally will be considered to be a qualified foreign corporation with respect to any dividend it pays on shares of stock that are readily tradable on an established securities market in the United States. We expect that our common shares will be listed and readily tradable on the New York Stock Exchange, which is an established securities market in the United States. However, there can be no assurance that our common shares will be considered readily tradable on an established securities market in the United States. However, there can be no assurance that our common shares will be considered readily tradable on an established securities market in the United States in later years. If they are, and subject to the discussion under "Passive Foreign Investment Company Considerations," below, such dividends paid by us will generally be "qualified dividend income" in the hands of individual U.S. holders, provided that a holding period requirement (more than 60 days of ownership, without protection from the risk of loss, during the 121-day period beginning 60 days before the ex-dividend date) and certain other requirements are met. Any dividend income that a U.S. holder realizes generally will be treated as foreign source income for foreign tax credit limitation purposes and generally will constitute passive category income. Dividends paid on our common shares will not be eligible for the dividends received deduction allowed to corporate U.S. holders.

#### Sale, Exchange or Other Taxable Disposition of our Common Shares

A U.S. holder will generally recognize gain or loss for U.S. federal income tax purposes upon the sale, exchange or other taxable disposition of our common shares in an amount equal to the difference between the U.S. dollar value of the amount realized from such sale or exchange (i.e., the amount of cash plus the fair market value of any property received) and the U.S. holder's tax basis for those common shares. Subject to the discussion under "Passive Foreign Investment Company Considerations," below, this gain or loss will generally be a capital gain or loss. The initial tax basis in the common shares generally will be equal to the cost of such common shares. Capital gain from the sale, exchange or other taxable disposition of our common shares by a non-corporate U.S. holder is generally eligible for a preferential rate of taxation applicable to capital gains, if the non-corporate U.S. holder's holding period determined at the time of such sale, exchange or other taxable disposition for such common shares exceeds one year (i.e., such gain is long-term taxable gain and will be taxable at ordinary income rates if not long-term capital gain). The deductibility of capital losses for U.S. federal income tax purposes is subject to limitations under the Code. Any such gain or loss that a U.S. holder recognizes generally will be treated as U.S. source income or loss for foreign tax credit limitation purposes. U.S. holders are encouraged to consult their own tax advisors regarding the availability of the U.S. foreign tax credit in their particular circumstances.

#### Medicare Tax

Certain U.S. holders that are individuals, estates or trusts and whose income exceeds certain thresholds are subject to a 3.8% tax on all or a portion of their "net investment income," which may

include all or a portion of their dividend income and net gains from the disposition of our common shares. Each U.S. holder that is an individual, estate or trust is urged to consult its tax advisors regarding the applicability of the Medicare tax to its income and gains in respect of its investment in our common shares.

## **Passive Foreign Investment Company Considerations**

We do not believe we were a PFIC for our taxable year ended December 31, 2016 and based on the current and anticipated value of our assets and the composition of our income, assets and operations, we do not expect to be a PFIC for the current taxable year or the foreseeable future. However, the application of the PFIC rules is subject to uncertainty in several respects, and therefore we cannot provide any assurance regarding our PFIC status for any past, current or future taxable years. A non-U.S. corporation will be classified as a PFIC for any taxable year in which, after applying certain look-through rules, either (i) at least 75% of its gross income is passive income; or (ii) at least 50% of the average quarterly value of its total gross assets (which, after this offering may be determined in part by reference to the quarterly market value of our common shares, which may be volatile) is attributable to assets that produce passive income or are held for the production of passive income. Moreover, for purposes of determining if a non-U.S. corporation is a PFIC, if the non-U.S. corporation owns, directly or indirectly, at least 25%, by value, of the shares of another corporation, it will be treated as if it holds directly its proportionate share of the assets and receives directly its proportionate share of the income of such other corporation.

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 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 this offering.

If we are classified as a PFIC for any taxable year during which a U.S. holder owns our common shares, the U.S. holder, absent certain elections (including the Purging Election and the Mark-to-Market Election described below), generally will be subject to special, adverse tax rules (regardless of whether we continue to be clssified as a PFIC) with respect to (a) any "excess distribution" (generally, any distributions received by the U.S. holder on its common shares in a taxable year that are greater than 125% of the average annual distributions received by the U.S. holder in the three preceding taxable years or, if shorter, the U.S. holder's holding period for its common shares) and (b) any gain realized from a sale or other disposition (including a pledge) of its common shares. Under these special tax rules (i) the excess distribution or gain will be allocated ratably over a U.S. holder's holding period for the common shares, (ii) the amount allocated to the current taxable year, and any taxable year prior to the first taxable year in which we became a PFIC, will be treated as ordinary income, and (iii) the amount allocated to each other year will be subject to the highest tax rate in effect for that year and the interest charge generally applicable to underpayments of tax will be imposed on the resulting tax attributable to each such year. If we are classified as a PFIC in any year with respect to which a U.S. holder owns our common shares, absent the "purging" election described below, we will continue to be treated as a PFIC with respect to such U.S. holder in all succeeding years during which the U.S. holder owns our common shares, absent the "purging" election described below, we will continue to be treated as a PFIC with respect to such U.S. holder in all succeeding years during which the U.S. holder owns our common shares, regardless of whether we continue to meet the tests described above.

Certain elections may be available to a U.S. holder that would result in alternative treatments. If we are a PFIC at any time when a U.S. holder holds our common shares, we will generally continue to be treated as a PFIC with respect to the U.S. holder for all succeeding years during which the U.S. holder holds our common shares even if we cease to qualify as a PFIC under the income and asset tests described above. However, if we cease to meet these tests, a U.S. holder can avoid the continuing impact of the PFIC

rules by making a special election (a "Purging Election") to recognize gain in the manner described above as if our common shares had been sold on the last day of the last taxable year during which we were a PFIC. In addition, for a U.S. holder making such an election, a new holding period would be deemed to begin for our common shares for purposes of the PFIC rules. After the Purging Election, the common shares with respect to which the Purging Election was made would not be treated as shares in a PFIC unless we were subsequently to qualify as a PFIC. U.S. holders should consult their tax advisers regarding the potential availability of a Purging Election that would allow them to eliminate PFIC status under certain circumstances.

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" 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.

Alternatively, a U.S. holder of "marketable stock" (as defined below) in a PFIC may make a mark-to-market election ("Mark-to-Market Election") with respect to such stock to elect out of the tax treatment discussed above. A Mark-to-Market Election generally is effective for the taxable year in which it is made and all subsequent years and cannot be revoked without the consent of the IRS. An electing U.S. holder generally would take into account as ordinary income, for each year that we are a PFIC, the excess of the fair market value of our common shares held at the end of the taxable year over the U.S. holder's adjusted tax basis in such common shares at that time. The U.S. holder would also take into account, as an ordinary loss for each year that we are a PFIC, the excess of the U.S. holder's adjusted tax basis in such common shares at the end of the taxable year over the fair market value of the shares at that time, but only to the extent of the aggregate of the amounts previously included in income as a result of the Mark-to-Market Election. The U.S. holder's tax basis in our common shares would be adjusted to reflect any income or loss resulting from the Mark-to-Market Election. Any gain from a sale, exchange or other disposition of the common shares in any taxable year in which we are a PFIC would be treated as ordinary income and any loss from such sale, exchange or other disposition would be treated first as ordinary loss to the extent of any net mark-to-market gains previously included in income and thereafter as capital loss. If, after having been a PFIC for one or more taxable years, we cease to be classified as a PFIC, the U.S. holder would not be required to take into account any latent gain or loss in the manner described above and any realized gain or loss would be classified as a capital gain or loss. A Mark-to-Market Election will not apply to our common shares for any taxable year during which we are not a PFIC, but it will remain in effect with respect to any subsequent taxable year in which we become a PFIC. Such election will not apply to any subsidiary that we own. A Mark-to-Market Election is available to a U.S. holder only if the common shares are considered "marketable stock." Generally, stock will be considered marketable stock if it is "regularly traded" on a "qualified exchange" within the meaning of applicable U.S. Treasury Regulations. A class of stock is regularly traded during any calendar year during which such class of stock is traded, other than in de minimis quantities, on at least 15 days during each calendar quarter. We expect that our common shares will be marketable stock as long as they remain listed on the New York Stock Exchange and are regularly traded. There can be no assurance that our common shares will continue to be so traded. U.S. holders should consult their tax advisers regarding the availability and advisability of making a Mark-to-Market Election in their particular circumstances.

Moreover, if we are treated as a PFIC with respect to any taxable year, to the extent any of our subsidiaries are also PFICs, a U.S. holder may be deemed to own shares in such lower-tier PFICs, and an election for mark-to-market treatment would likely not be available with respect to any such subsidiaries. U.S. holders are urged to consult their own tax advisors regarding the application of the PFIC rules to any of our subsidiaries.

If we are a PFIC with respect to a U.S. holder of our common shares, such U.S. holder will generally be required to file an annual information return on IRS Form 8621 with respect to our common shares and the shares of any of subsidiaries that also qualify as a PFIC. U.S. holders should consult their own tax advisers concerning annual filing requirements.

NO ASSURANCE CAN BE GIVEN REGARDING OUR PFIC STATUS FOR ANY PAST, CURRENT OR FUTURE TAXABLE YEARS. U.S. HOLDERS SHOULD CONSULT THEIR OWN TAX ADVISORS WITH RESPECT TO THE OPERATION OF THE PFIC RULES AND RELATED REPORTING REQUIREMENTS IN LIGHT OF THEIR PARTICULAR CIRCUMSTANCES, INCLUDING THE ADVISABILITY OF MAKING ANY ELECTION THAT MAY BE AVAILABLE.

## **Backup Withholding and Information Reporting**

U.S. holders generally will be subject to information reporting requirements with respect to dividends on our common shares and on the proceeds from the sale, exchange or disposition of our common shares that are paid within the United States or through U.S.-related financial intermediaries, unless the U.S. holder is an "exempt recipient." In addition, U.S. holders may be subject to backup withholding on such payments, unless the U.S. holder provides a taxpayer identification number and a duly executed IRS Form W-9 or otherwise establishes an exemption. Backup withholding is not an additional tax, and the amount of any backup withholding will be allowed as a credit against a U.S. holder's U.S. federal income tax liability and may entitle such holder to a refund, provided that the required information is timely furnished to the IRS.

## Foreign Asset Reporting

Certain U.S. holders (and to the extent provided in IRS guidance, certain non-U.S. holders) who hold interests in "specified foreign financial assets" (as defined in Section 6038D of the Code) are generally required to file an IRS Form 8938 as part of their U.S. federal income tax returns with information relating to such assets for each taxable year in which the aggregate value of all such assets exceeds \$75,000 at any time during the taxable year or \$50,000 on the last day of the taxable year (or such higher dollar amount as prescribed by applicable IRS guidance). "Specified foreign financial assets" generally include, among other assets, financial accounts maintained by foreign financial institutions, and our common shares, unless the shares are held through an account maintained by a financial institution. Substantial penalties may apply to any failure to timely file a complete and correct IRS Form 8938. Additionally, in the event an applicable U.S. holder (and to the extent provided in IRS guidance, a non-U.S. holder) that is required to file IRS Form 8938 either fails to file or fails to report a relevant asset, the statute of limitations on the assessment and collection of U.S. federal income taxes of such holder for the related tax year may not close until three years after the date that the required information is filed. Prospective investors are encouraged to consult with their own tax advisors regarding the possible reporting obligations under these and other disclosure requirements in light of their individual circumstances.

THE DISCUSSION ABOVE IS A GENERAL SUMMARY. IT DOES NOT COVER ALL TAX MATTERS THAT MAY BE OF IMPORTANCE TO A PROSPECTIVE INVESTOR. EACH PROSPECTIVE INVESTOR IS URGED TO CONSULT ITS OWN TAX ADVISOR ABOUT THE TAX CONSEQUENCES TO IT OF AN INVESTMENT IN OUR COMMON SHARES IN LIGHT OF THE INVESTOR'S OWN CIRCUMSTANCES.

# UNDERWRITING

Under the terms and subject to the conditions contained in an underwriting agreement dated the date of this prospectus, the underwriters named below, for whom Morgan Stanley & Co. LLC and Piper Jaffray & Co. are acting as representatives, have severally agreed to purchase, and we have agreed to sell to them, severally, the number of shares indicated below:

Name	Number of Shares
Morgan Stanley & Co. LLC	3,960,000
Piper Jaffray & Co.	2,772,000
Barclays Capital Inc.	1,485,000
William Blair & Company, L.L.C.	1,188,000
Needham & Company, LLC	495,000
Total	9,900,000

The underwriters and the representatives are collectively referred to as the "underwriters" and the "representatives," respectively. The underwriters are offering the common shares subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the several underwriters to pay for and accept delivery of the common shares offered by this prospectus are subject to the approval of certain legal matters by their counsel and to certain other conditions. The underwriters are obligated to take and pay for all of the common shares offered by this prospectus if any such shares are taken. However, the underwriters are not required to take or pay for the shares covered by the underwriters' over-allotment option described below.

The underwriters initially propose to offer part of the common shares directly to the public at the public offering price listed on the cover page of this prospectus and part to certain dealers at a price that represents a concession not in excess of \$0.714 per share under the public offering price. After the initial offering of the common shares, the offering price and other selling terms may from time to time be varied by the representatives.

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to 1,485,000 additional common shares at the public offering price listed on the cover page of this prospectus, less underwriting discounts and commissions. The underwriters may exercise this option solely for the purpose of covering over-allotments, if any, made in connection with the offering of the common shares offered by this prospectus. To the extent the option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase about the same percentage of the additional common shares as the number listed next to the underwriter's name in the preceding table bears to the total number of common shares listed next to the names of all underwriters in the preceding table.

Certain of our existing principal shareholders, directors and their affiliated entities have agreed to purchase an aggregate of 3,142,117 common shares in this offering at the initial public offering price per share. The underwriters will receive the same underwriting discount on the shares purchased by these entities as they will on the other shares sold to the public in this offering.

The following table shows the per share and total public offering price, underwriting discounts and commissions, and proceeds before expenses to us. These amounts are shown assuming both no exercise

and full exercise of the underwriters' over-allotment option to purchase up to an additional

common shares.

			Т	otal	
	Per Share		No Exercise		Full Exercise
Public offering price	\$ 17.00	) §	5 168,300,000	\$	193,545,000
Underwriting discounts and commissions	\$ 1.19	) §	11,781,000	\$	13,548,150
Proceeds, before expenses	\$ 15.8	\$	5 156,519,000	\$	179,996,850

The estimated offering expenses payable by us, exclusive of the underwriting discounts and commissions, are approximately \$3.6 million. We have agreed to reimburse the underwriters up to \$30,000 for expenses relating to clearance of this offering with the Financial Industry Regulatory Authority.

The underwriters have informed us that they do not intend sales to discretionary accounts to exceed 5% of the total number of common shares offered by them.

Our common shares have been approved for listing on the New York Stock Exchange under the trading symbol "BHVN."

At our request, the underwriters have reserved for sale at the initial public offering price per share up to 495,000 common shares, or 5% of the common shares offered by this prospectus, to certain individuals through a directed share program, including employees, directors and other persons associated with us. If purchased by these persons, these shares will not be subject to a lock-up restriction, except in the case of shares purchased by any director or officer, which will be subject to the lock-up restrictions described below. The number of common shares available for sale to the general public will be reduced by the number of reserved shares sold to these individuals. Any reserved shares not purchased by these individuals will be offered by the underwriters to the general public on the same basis as the other common shares offered under this prospectus. The directed share program will be arranged through Morgan Stanley & Co. LLC.

We and all of our directors and officers and the holders of substantially all of our outstanding stock and stock options have agreed that, without the prior written consent of Morgan Stanley & Co. LLC on behalf of the underwriters, we and they will not, during the period ending 180 days after the date of this prospectus, or the restricted period:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any common shares or any securities convertible into or exercisable or exchangeable for common shares; or
- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the common shares;

whether any such transaction described above is to be settled by delivery of common common shares or such other securities, in cash or otherwise, or publicly disclose the intention to do any of the foregoing. In addition, without the prior written consent of Morgan Stanley & Co. LLC on behalf of the underwriters, (i) our directors and officers and such holders will not, during the restricted period, make any demand for, or exercise any right, or publicly disclose its intention to make any demand or exercise any right, with respect to the registration of any common shares or any security convertible into or exercisable or exchangeable for common shares and (ii) we will not file any registration statement with the Securities and Exchange Commission relating to the offering of any common shares or any securities convertible into or exercise and such holders agreed and consented to the entry of stop transfer instructions with our transfer agent and registrar against the transfer of each such person's common shares except in compliance with the below restrictions.

The restrictions described in the immediately preceding paragraph to do not apply to:

- transactions relating to common shares or other securities acquired in open market transactions after the completion of our initial public offering, provided that no filing under Section 16(a) of the Exchange Act reporting a reduction in beneficial ownership of common shares is required or is voluntarily made during the restricted period;
- transfers of common shares or any security convertible into common shares to an immediate family member or a trust for the direct or indirect benefit of the undersigned or such immediate family member of the undersigned (for purposes of the foregoing, "immediate family" means any relationship by blood, marriage, civil union, domestic partnership or adoption, not more remote than first cousin), provided that each transferee signs and delivers a lock-up agreement, and provided that no filing under Section 16(a) of the Exchange Act reporting a reduction in beneficial ownership of common shares is required or is voluntarily made during the restricted period;
- transfers of common shares or any security convertible into common shares as a bona fide gift or charitable contribution, provided that each donee signs and delivers a lock-up agreement, and provided that no filing under Section 16(a) of the Exchange Act reporting a reduction in beneficial ownership of common shares shall be required or shall be voluntarily made during the restricted period;
- transfers of common shares or any security convertible into common shares by will or intestacy, provided that each transferee signs and delivers a lock-up agreement, and provided that no filing under Section 16(a) of the Exchange Act reporting a reduction in beneficial ownership of common shares is required or is voluntarily made during the restricted period;
- if the transferor is a corporation, partnership or other business entity, distributions of common shares or any security convertible into common shares to limited partners, members, stockholders or holders of similar equity interests in the transferor, provided that each distribute signs and delivers a lock-up agreement, and provided that no filing under Section 16(a) of the Exchange Act reporting a reduction in beneficial ownership of common shares is required or is voluntarily made during the restricted period;
- if the transferor is a trust, transfers or distributions of common shares or any securities convertible into or exercisable or exchangeable for common shares to a trustor or beneficiary of the trust or to the estate of a beneficiary of such trust, provided that each transfere signs and delivers a lock-up agreement, and provided that no filing under Section 16(a) of the Exchange Act reporting a reduction in beneficial ownership of common shares is required or is voluntarily made during the restricted period;
- the exercise of a stock option granted under a stock incentive plan or stock purchase plan described in this prospectus, and the receipt from the Company of common shares upon such exercise, insofar as such option is outstanding as of the date of the lock-up agreement or date of this prospectus, provided that the underlying shares shall continue to be subject to the restrictions on transfer set forth in the lock-up agreement, and provided that, if required, any public report or filing under Section 16 of the Exchange Act clearly indicates in the footnotes thereto that the filing relates to the exercise of a stock option, that no common shares were sold by the reporting person and that the common shares received upon exercise of the stock option are subject to a lock-up agreement with the underwriters;
- the disposition of common shares to us, or the withholding of common shares by us, in a transaction exempt from Section 16(b) of the Exchange Act solely to the extent required for the payment of taxes due with respect to the vesting or expiration of options or the vesting of restricted stock or restricted stock units granted under a stock incentive plan, stock purchase plan or pursuant to a contractual employment arrangement described in this prospectus, insofar as such options,

restricted stock or restricted stock units are outstanding as of the date of the lock-up agreement or as of the date of this prospectus, provided that no filing under Section 16(a) of the Exchange Act reporting a reduction in beneficial ownership of common shares is required or is voluntarily made during the restricted period;

- transfers to us in connection with the repurchase of common shares in connection with the termination of the person's employment with us pursuant to contractual agreements with us as in effect as of the date of this prospectus, provided that no filing under Section 16(a) of the Exchange Act reporting a reduction in beneficial ownership of common shares is required or is voluntarily made during the restricted period;
- transfers of common shares or any security convertible into or exercisable or exchangeable for common shares pursuant to a domestic order, divorce decree or court order, provided that each transferee signs and delivers a lock-up agreement, and provided that, if required, any public report or filing under Section 16 of the Exchange Act shall clearly indicate in the footnotes thereto that the filing relates to the transfer of such securities pursuant to a domestic order, divorce decree or court order, that no such securities were sold by the reporting person and that the securities so transferred are subject to a lock-up agreement with the underwriters;
- the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of common shares, provided that (i) such plan does not provide for the transfer of common shares during the restricted period and (ii) to the extent a public announcement or filing under the Exchange Act, if any, is required of or voluntarily made by or on behalf of the person or us regarding the establishment of such plan, such announcement or filing shall include a statement to the effect that no transfer of common shares may be made under such plan during the restricted period; or
- a merger, consolidation or other similar transaction, occurring after the closing of the offering, in which all holders of the common shares may participate, involving a change of control of the Company and approved by our board of directors, provided that, in the event that such change-of-control transaction is not completed, the person's shares shall remain subject to the restrictions contained in the lock-up agreement and title to the person's shares shall remain with the person (for purposes of the foregoing, "change of control" means the transfer (whether by tender offer, merger, consolidation or other similar transaction), in one transaction or a series of related transactions, to a person or group of affiliated persons (other than an underwriter pursuant to the offering), of the our voting securities if, after such transfer, such person or group of affiliated persons would hold at least 90% of our or the surviving entity's outstanding voting securities).

The representatives, in their sole discretion, may release the common shares and other securities subject to the lock-up agreements described above at any time.

In order to facilitate this offering of the common shares, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common shares. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting agreement, creating a short position. A short sale is covered if the short position is no greater than the number of shares available for purchase by the underwriters under the over-allotment option. The underwriters can close out a covered short sale by exercising the over-allotment option or purchasing shares in the open market. In determining the source of shares to close out a covered short sale, the underwriters will consider, among other things, the open market price of shares compared to the price available under the over-allotment option. The underwriters may also sell shares in excess of the over-allotment option, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common shares in the open market after pricing that could adversely affect investors who purchase in this offering. As an additional means of facilitating this offering,

the underwriters may bid for, and purchase, common shares in the open market to stabilize the price of the common shares. These activities may raise or maintain the market price of the common shares above independent market levels or prevent or retard a decline in the market price of the common shares. The underwriters are not required to engage in these activities and may end any of these activities at any time.

We and the underwriters have agreed to indemnify each other against certain liabilities, including liabilities under the Securities Act.

A prospectus in electronic format may be made available on websites maintained by one or more underwriters, or selling group members, if any, participating in this offering. The representatives may agree to allocate a number of common shares to underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters that may make Internet distributions on the same basis as other allocations.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their respective affiliates have, from time to time, performed, and may in the future perform, various financial advisory and investment banking services for us, for which they received or will receive customary fees and expenses.

William Blair & Company, L.L.C., or William Blair, served as one of our placement agents in connection with our Series A preferred share financing in October 2016. As a component of its compensation for serving as placement agent, William Blair received 26,235 Series A preferred shares at the closing of the first tranche of such financing, which occurred in October 2016, and received an additional 26,235 Series A preferred shares at the closing of the second tranche of such financing, which occurred in February 2017. FINRA deems the Series A preferred shares William Blair received in the second tranche underwriting compensation. The Series A preferred shares William Blair received in the first tranche are excluded from underwriting compensation pursuant to FINRA Rule 5110 (d)(5)(C). Pursuant to FINRA Rule 5110(g)(1), none of the shares received by William Blair in the first tranche or the second tranche may be sold during this offering, or sold, transferred, assigned, pledged or hypothecated, or be the subject of any hedging, short sale, derivative, put or call transaction that would result in the effective economic disposition of these shares by any person for a period of 180 days immediately following the date of the effectiveness or commencement of sales of this offering, subject to certain exceptions set forth in FINRA Rule 5110(g)(2).

In addition, in the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investment and securities activities may involve our securities and instruments. The underwriters and their respective affiliates may also make investment recommendations or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long or short positions in such securities and instruments.

# **Pricing of the Offering**

Prior to this offering, there has been no public market for our common shares. The initial public offering price was determined by negotiations among us and the representatives. Among the factors considered in determining the initial public offering price were our future prospects and those of our industry in general, our sales, earnings and certain other financial and operating information in recent periods, and the price-earnings ratios, price-sales ratios, market prices of securities, and certain financial and operating information of companies engaged in activities similar to ours.

## **Selling Restrictions**

## Canada

The common shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the common shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws. Furthermore, as residents of Canada will own more than 10% the outstanding common shares after giving effect to this initial public offering, a Canadian purchaser will not be able to rely on the exemption from the prospectus requirements available in respect of certain resales outside of Canada found in section 2.14 of National Instrument 45-102—Resale of Securities.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 *Underwriting Conflicts* (**NI 33-105**), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

## European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive, each, a Relevant Member State, an offer to the public of any of our common shares may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of any of our common shares may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

- to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives for any such offer; or
- in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of our common shares shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to any of our common shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any of our common shares to be offered so as to enable an investor to decide to purchase any of our common shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression "Prospectus Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State, and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

# **United Kingdom**

Each underwriter has represented and agreed that:

- it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000, or FSMA, received by it in connection with the issue or sale of our common shares in circumstances in which Section 21(1) of the FSMA does not apply to us; and
- it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to our common shares in, from or otherwise involving the United Kingdom.

# **LEGAL MATTERS**

The validity of the common shares and certain other matters of British Virgin Islands law will be passed upon for us by Maples and Calder, our special BVI counsel. Certain other legal matters will be passed upon for us by Cooley LLP, Reston, Virginia, and for the underwriters by Ropes & Gray LLP, Boston, Massachusetts.

# EXPERTS

The financial statements as of December 31, 2015 and 2016 and for each of the two years in the period ended December 31, 2016 included in this prospectus have been so included in reliance on the report (which contains an explanatory paragraph relating to the Company's ability to continue as a going concern as described in Note 1 to the financial statements) of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

#### WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act, with respect to the common shares being offered by this prospectus. This prospectus, which constitutes part of the registration statement, does not contain all of the information in the registration statement and its exhibits. For further information with respect to our company and the common shares offered by this prospectus, we refer you to the registration statement and its exhibits. Statements contained in this prospectus as to the contents of any contract or any other document referred to are not necessarily complete, and in each instance, we refer you to the copy of the contract or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference.

You can read our SEC filings, including the registration statement, over the internet at the SEC's website at *www.sec.gov*. You may also read and copy any document we file with the SEC at its public reference room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You may also obtain copies of these documents at prescribed rates by writing to the Public Reference Section of the SEC at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference facilities.

Upon completion of this offering, we will be subject to the information reporting requirements of the Exchange Act, and we will file reports, proxy statements and other information with the SEC. These reports, proxy statements and other information will be available for inspection and copying at the public reference room and website of the SEC referred to above. We also maintain a website at *www.biohavenpharma.com*, at which you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is not part of, and is not incorporated into, this prospectus.

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## **REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

To the Board of Directors and Shareholders of Biohaven Pharmaceutical Holding Company Ltd.

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of operations and comprehensive loss, of convertible preferred shares and shareholders' equity (deficit) and of cash flows present fairly, in all material respects, the financial position of Biohaven Pharmaceutical Holding Company Ltd. and its subsidiaries as of December 31, 2015 and 2016, and the results of their operations and their cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these financial statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has incurred recurring losses from operations since inception, has an accumulated deficit, and will require additional financing to fund future operations. These circumstances raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

/s/ PricewaterhouseCoopers LLP

Hartford, Connecticut April 3, 2017

# **CONSOLIDATED BALANCE SHEETS**

# (Amounts in thousands, except share and per share amounts)

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Total liabilities, convertible preferred shares and shareholders'				_	(45.022)		17.175
			1,087	-	(45,033)		17,175
equity (deficit) $\frac{1,892}{27,017} = \frac{27,017}{27,017}$		¢	1.002	¢	07.017	¢	07.017
	equity (deficit)	\$	1,892	\$	27,017	\$	27,017

The accompanying notes are an integral part of these consolidated financial statements.

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# CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

# (Amounts in thousands, except share and per share amounts)

		Year Decem		
		2015		2016
Operating expenses:				
Research and development	\$	7,559	\$	55,529
General and administrative		2,137		5,109
Total operating expenses		9,696		60,638
Loss from operations		(9,696)		(60,638)
Other income (expense):				
Interest expense				(385)
Change in fair value of warrant liability				154
Change in fair value of derivative liability		(370)		(65)
Change in fair value of contingent equity liability		_		(2,263)
Loss from equity method investment				(247)
Total other income (expense), net		(370)		(2,806)
Loss before provision for income taxes		(10,066)		(63,444)
Provision for income taxes				90
Net loss and comprehensive loss		(10,066)		(63,534)
Less: Net income (loss) attributable to non-controlling interests		(4)		143
Net loss attributable to common shareholders of Biohaven Pharmaceutical				
Holding Company Ltd.	\$	(10,062)	\$	(63,677)
Net loss per share attributable to common shareholders of Biohaven	_		-	
Pharmaceutical Holding Company Ltd.—basic and diluted	\$	(0.91)	\$	(5.05)
Weighted average common shares outstanding—basic and diluted	_	11,009,277	-	12,608,366
	_	11,009,277	-	12,000,000
Pro forma net loss per share attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd.—basic and diluted (unaudited)			\$	(4.48)
			-	(10)
Pro forma weighted average common shares outstanding—basic and diluted (unaudited)			_	14,215,323

The accompanying notes are an integral part of these consolidated financial statements.

# CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED SHARES AND SHAREHOLDERS' EQUITY (DEFICIT)

	Series Convert Preferi	A tible red	housands, exc			er share ar Note Receivable		Total Biohaven Pharmaceutical Holding Company Ltd. Shareholders'	Non-	Total Shareholders
	Share		Common Sl Shares		Paid-in	from	Accumulated Deficit	Equity (Deficit)	Controlling	Equity
Balances as of December 31, 2014		Amount \$ —	10,652,000 S	Amount § 3,587	•	Shareholder \$ (500)			Interests \$ (53)	(Deficit) \$ 1,507
Issuance of common shares, net of offering costs of \$37		_	867,000	4,816	_	_	_	4,816	_	4,816
Issuance of common shares in connection with license agreement										
(Note 13) Issuance of common share warrant in connection with license	_	_	50,000	262	_	_	_	262		262
agreement (Note 13) Collection of note receivable from	_	_	—	_	1,231	_		1,231	_	1,231
share-based compensation	_	—	—	—	—	500	—	500	—	500
expense Net loss Balances as of					2,837		(10,062)	2,837 (10,062)	(4)	2,837 (10,066
December 31, 2015 Issuance of		—	11,569,000	8,665	4,258		(11,779)	1,144	(57)	1,087
common shares, net of offering costs of \$120 Issuance of common share warrant	_	_	1,519,500	11,279		_	_	11,279	_	11,279
in connection with license agreement (Note 13) Issuance of Series A convertible preferred shares, net of cash offering	4,305,209	38,270		_	2,127	Ξ	Ξ	2,127	Ξ	2,127

costs of \$1,730 Issuance of Series A convertible preferred shares as payment of related offering costs Issuance of Series A convertible preferred shares in settlement of contingent equity liability	105,010	_			_			_		_
(Note 13)	538,150	5,000					_			
Acquisition of BPI (Note 18) Share-based	—	—			(509)	—	—	(509)	(86)	(595
compensation expense Net loss					4,603		(63,677)	4,603 (63,677)	143	4,603 (63,534
Balances as of December 31, 2016	4,948,369	543,270	13,088,500	\$19,944	<u>\$ 10,479</u> \$	\$	(75,456)\$	(45,033)\$	\$	(45,033

The accompanying notes are an integral part of these consolidated financial statements.

# CONSOLIDATED STATEMENTS OF CASH FLOWS

# (Amounts in thousands, except share and per share amounts)

	Yes Decc 2015		
Cash flows from operating activities:	2015		2010
Net loss	\$ (10.06	6) \$	63,534)
Adjustments to reconcile net loss to net cash used in operating activities:	φ (10,00	<i>σ</i>	(05,551)
Share-based compensation expense	2,83	7	4,603
Depreciation expense		2	5
Non-cash interest expense	_	_	374
Benefit from deferred income taxes	_	_	(9)
Fair value of contingent equity liability under license agreements	_	_	21,675
Issuance of common shares as consideration for license agreement	26	2	
Fair value of warrants issued as consideration for license agreement	1.23		2,127
Change in fair value of warrant liability	1,20	_	(154)
Change in fair value of derivative liability	37	0	65
Change in fair value of contingent equity liability	_	_	2,263
Loss from equity method investment	_	_	247
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	(42)	3)	24
Accounts payable	2	1	678
Accrued expenses	13		2,148
Other long-term liabilities		7	(16)
Net cash used in operating activities	(5,62	_	(29,504)
	(5,02		(2),504)
Cash flows from investing activities: Purchases of property and equipment	(	3)	(26)
Purchase of equity method investment	(	)	(3,000)
Increase in restricted cash			(127)
	(	$\frac{1}{2}$ -	
Net cash used in investing activities	(	3)	(3,153)
Cash flows from financing activities:			40.000
Proceeds from issuance of Series A convertible preferred shares	4.05	-	40,000
Proceeds from issuance of common shares	4,85		11,399
Payments of offering costs	(3	/)	(1,507)
Proceeds from issuance of notes payable	_	-	5,000
Payments of debt issuance costs		-	(197)
Collection of note receivable from shareholder	50	J	_
Advanced payment received for the second closing of Series A convertible			(7
preferred shares		<u> </u>	67
Net cash provided by financing activities	5,31		54,762
Net increase (decrease) in cash	(31)		22,105
Cash at beginning of year	1,77	-	1,460
Cash at end of year	\$ 1,46	0 \$	23,565
Supplemental disclosure of cash flow information:			
Cash paid for interest	\$ -	- \$	11
Supplemental disclosure of non-cash investing and financing activities:			
Deferred offering costs included in accrued expenses	\$ -	- \$	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
Issuance of Series A convertible preferred shares in settlement of contingent equity			
liability	\$ -	- \$	5,000
Issuance of Series A convertible preferred shares as payment of related offering			
costs	\$ -	- \$	975
Issuance of notes payable to related parties in connection with acquisition of BPI	\$ –	- \$	595

The accompanying notes are an integral part of these consolidated financial statements.

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# 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. (the "Company") was incorporated in Tortola, British Virgin Islands in September 2013. The Company is a clinical-stage biopharmaceutical company with a portfolio of innovative, late-stage product candidates targeting neurologic diseases, including rare disorders. The Company's product candidates are small molecules based on two distinct mechanistic platforms—calcitonin gene-related peptide ("CGRP") receptor antagonists and glutamate modulators—which the Company believes have the potential to significantly alter existing treatment approaches across a diverse set of neurological indications with high unmet need in both large markets 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 treatment of migraine and for which it intends to initiate two Phase 3 clinical trials in the second half of 2017. The most advanced product candidate from the Company's glutamate modulation platform is trigriluzole, which the Company is developing for the treatment of ataxias with an initial focus on spinocerebellar ataxia ("SCA"). The Company has received orphan drug designation from the U.S. Food and Drug Administration ("FDA") for trigriluzole in SCA, and the Company began a Phase 2/3 clinical trial in SCA in December 2016. The Company's second most advanced product candidate from its glutamate modulation platform is BHV-0223, which the Company is developing for the treatment of anyotrophic lateral sclerosis ("ALS"), a neurodegenerative disease that affects nerve cells in the brain and spinal cord. The Company has received orphan drug designation from the LS.

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 require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

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 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 (see Note 17). BPI is a contract research organization ("CRO") whose only customer is the Company. Since its incorporation, 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 funding for the operations of BPI was provided by the Company. The Company has 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. Accordingly, 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

# NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

## 1. Nature of the Business and Basis of Presentation (Continued)

commenced any operations. For periods prior to December 31, 2016, 100% of the equity in BPI was reflected as non-controlling interest within shareholders' deficit on the consolidated balance sheet. On December 31, 2016, the Company acquired 100% of the issued and outstanding shares of BPI (see Note 18), and as a result, for periods subsequent to the acquisition, the Company no longer reports any non-controlling interest related to BPI.

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 as well as BPI, a variable interest entity, after elimination of all significant intercompany accounts and transactions.

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.

## **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.

Through December 31, 2016, the Company has funded its operations primarily with proceeds from sales of preferred and common shares and borrowings under a credit agreement. The Company has incurred recurring losses since its inception, including net losses of \$10,066 and \$63,534 for the years ended December 31, 2015 and 2016, respectively. In addition, as of December 31, 2016, the Company had an accumulated deficit of \$75,456. The Company expects to continue to generate operating losses for the foreseeable future. As of April 3, 2017, the issuance date of these consolidated financial statements, the Company expects that its cash of \$23,565 as of December 31, 2016, together with the \$38,635 of net cash proceeds received from the second closing of the Company's sale of Series A convertible preferred shares ("Series A preferred shares") in February 2017 (see Note 20), will be sufficient to fund its operating expenses, capital expenditure requirements and debt service payments through July 31, 2017. The future viability of the Company beyond that point is dependent on its ability to raise additional capital to finance its operations.

The Company is seeking to complete an initial public offering of its common shares. In the event the Company does not complete an initial public offering, the Company expects to seek additional funding through private equity financings, 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, or the Company may be

# NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

## 1. Nature of the Business and Basis of Presentation (Continued)

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.

Based on its recurring losses from operations incurred since inception, expectation of continuing operating losses for the foreseeable future, and need to raise additional capital to finance its future operations, the Company has concluded that there is substantial doubt about its ability to continue as a going concern within one year after the date that the consolidated financial statements are issued.

The accompanying consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty. Accordingly, the consolidated financial statements have been prepared on a basis that assumes the Company will continue as a going concern and which contemplates the realization of assets and satisfaction of liabilities and commitments in the ordinary course of business.

## 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 and contingent equity instruments. 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.

#### **Unaudited Pro Forma Information**

The accompanying unaudited pro forma consolidated balance sheet as of December 31, 2016 has been prepared to give effect, upon the closing of a qualified initial public offering, to the conversion of all outstanding convertible preferred shares into 4,948,369 common shares and the issuance of an aggregate of 1,883,523 common shares to AstraZeneca AB ("AstraZeneca") and Bristol Myers-Squibb Company ("BMS") pursuant to the Company's license agreements with AstraZeneca and BMS (see Note 13) as if the proposed initial public offering had occurred on December 31, 2016.

In the accompanying consolidated statements of operations and comprehensive loss, the unaudited pro forma basic and diluted net loss per share attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd. for the year ended December 31, 2016 have been prepared to give effect, upon the closing of a qualified initial public offering, to the conversion of all outstanding convertible preferred shares into 4,948,369 common shares and the issuance of an aggregate of 1,883,523 common shares to AstraZeneca and BMS pursuant to the Company's license agreements with AstraZeneca and BMS (see Note 13) as if the proposed initial public offering had occurred on the latest of January 1, 2016,

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

## 2. Summary of Significant Accounting Policies (Continued)

the issuance date of the convertible preferred shares or the date the Company entered into each respective license agreement.

## **Restricted Cash**

As of December 31, 2016, current restricted cash consisted of \$67 of cash received from investors as an advance payment for their participation in the second closing of the Company's sale of Series A preferred shares and non-current restricted cash consisted of a \$60 certificate of deposit held as a security deposit in connection with the Company's corporate credit card.

## **Concentrations of Credit Risk**

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash. Periodically, the Company maintains deposits in accredited financial institutions in excess of federally insured limits. The Company deposits its cash in financial institutions that it believes have high credit quality and has not experienced any losses on such accounts and does not believe it is exposed to any unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

## **Deferred Offering Costs**

The Company capitalizes certain legal, professional accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After consummation of the equity financing, these costs are recorded in shareholders' equity (deficit) as a reduction of proceeds generated as a result of the offering. Should the planned equity financing be abandoned, the deferred offering costs will be expensed immediately as a charge to operating expenses in the consolidated statement of operations and comprehensive loss. The Company did not record any deferred offering costs as of December 31, 2015. The Company recorded deferred offering costs of \$134 as of December 31, 2016.

# **Equity Method Investments**

Investments in non-public companies in which the Company owns less than a 50% equity interest and where it exercises 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. The Company periodically reviews the carrying value of its investment 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, the financial condition and business prospects of the investee as well as the Company's intent with regard to the investment.

# NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

## 2. Summary of Significant Accounting Policies (Continued)

#### **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, 2015 and 2016, the Company's property and equipment consisted of computer equipment, which has an estimated useful life of three 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 charged to expense as incurred.

## Impairment of Long-Lived Assets

Long-lived assets consist of property and equipment. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset group for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset group to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset group are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset group over its fair value, determined based on discounted cash flows. To date, the Company has not recorded any impairment losses on long-lived assets.

## 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, determined according to the fair value hierarchy described above (see Note 3). The carrying values

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

## 2. Summary of Significant Accounting Policies (Continued)

of other current assets, accounts payable, accrued expenses and notes payable under a credit agreement 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 for the purposes of assessing performance and making operating decisions. The Company's singular current focus is on a pipeline of product candidates that represent two distinct mechanistic platforms—CGRP receptor antagonists, and glutamate modulators. 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, share-based compensation and benefits, facilities costs, depreciation, third-party license fees, and external costs of outside 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.

## **Research Contract Costs and Accruals**

The Company has entered into various research and development-related contracts with companies both inside and outside of the United States. 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. Significant 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.

## Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses.

## **Share-Based Compensation**

The Company measures stock options granted to employees and directors based on the fair value on the date of the grant and recognizes 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 has not issued any stock options with performance-based vesting conditions.

# NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

## 2. Summary of Significant Accounting Policies (Continued)

For share-based awards granted to consultants and non-employees, compensation expense is recognized over the period during which services are 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 is remeasured using the then-current fair value of the Company's common shares and updated assumption inputs in the Black-Scholes option-pricing model.

The Company classifies 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 historically has been a private company and lacks 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 (see Note 8), the Company agreed to issue warrants to purchase common shares to the guarantor and co-guarantor of its obligations under the agreement (see Note 8). 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 warrants are exercised, expire or qualify for equity classification.

## **Derivative Liability**

The Company's license agreement with Yale University ("Yale") (see Note 13) provides for a change-of-control payment to Yale upon the occurrence of a change-of-control event, as defined in the agreement, including an initial public offering. The Company classifies the change-of-control payment obligation as a liability on its consolidated balance sheet because it represents 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 derivative liability was initially recorded at fair value upon entering into the license agreement and is subsequently remeasured to fair value at each reporting date. Changes in the fair value of the derivative liability are recognized as a component of other income (expense), net in the consolidated statement of

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

## 2. Summary of Significant Accounting Policies (Continued)

operations and comprehensive loss. Changes in the fair value of the derivative liability will continue to be recognized until a change-ofcontrol event occurs.

## **Contingent Equity Liability**

The Company's license agreements with AstraZeneca and BMS (see Note 13) require the Company to issue shares of capital stock upon the occurrence of specified financing or change-of-control events or development milestones, as defined in the agreements. In each agreement, the class and number of shares to be issued upon a triggering event were not known upon entering into the license agreements; however, the dollar amount of the shares to be issued upon a triggering event is fixed. The Company classifies these contingent obligations to issue shares as a liability on its consolidated balance sheet because each represents an obligation to issue a variable number of shares for a fixed dollar amount. Each contingent equity liability was initially recorded at fair value upon entering into each respective agreement and is subsequently remeasured to fair value at each reporting date. Changes in the fair values of the contingent equity liabilities 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 contingent equity liabilities will continue to be recognized until the occurrence of a respective triggering event.

## **Comprehensive Loss**

Comprehensive loss includes net loss as well as other changes in shareholders' equity (deficit) that result from transactions and economic events other than those with shareholders. There was no difference between net loss and comprehensive loss for each of the periods presented in the accompanying consolidated financial statements.

#### **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 Company accounts for uncertainty in income taxes recognized in the consolidated financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the consolidated financial statements. The amount of the benefit that may be recognized is the largest amount that has a

# NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

## 2. Summary of Significant Accounting Policies (Continued)

greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

## Net Loss per Share Attributable to Common Shareholders of Biohaven Pharmaceutical Holding Company Ltd.

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.

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 entitle the holders of such shares to participate in dividends but contractually do not require the holders of such shares to participate in losses of the Company. Accordingly, in periods in which the Company reports a net loss attributable to common shareholders, diluted net loss per share attributable to common shareholders, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive.

## **Recently Adopted Accounting Pronouncements**

In March 2016, the Financial Accounting Standards Board ("FASB") issued ASU No. 2016-09, *Improvements to Employee Share-Based Payment Accounting* ("ASU 2016-09"). The new standard involves several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities and classification on the statement of cash flows. Certain of these changes are required to be applied retrospectively, while other changes are required to be applied prospectively. The new standard will be effective for the Company on January 1, 2017 with early adoption permitted. The Company has elected to early adopt ASU 2016-09 and has reflected the adoption in the consolidated financial statements of the Company. The adoption of ASU 2016-09 had no impact on the Company's financial position, results of operations or cash flows.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

## 2. Summary of Significant Accounting Policies (Continued)

In November 2015, the FASB issued ASU No. 2015-17, *Balance Sheet Classification of Deferred Taxes* ("ASU 2015-17"). ASU 2015-17 requires deferred tax liabilities and assets to be classified as non-current in the consolidated balance sheet. ASU 2015-17 is required to be adopted for annual periods beginning after December 15, 2016, including interim periods within those fiscal years. The amendment may be applied either prospectively to all deferred tax liabilities and assets or retrospectively to all periods presented. The Company elected to early adopt this guidance retrospectively to all periods presented, and its adoption had no impact on the Company's financial position, results of operations or cash flows.

In April 2015, the FASB issued ASU No. 2015-03, *Simplifying the Presentation of Debt Issuance Costs* ("ASU 2015-03"), which requires that debt issuance costs related to a debt liability be presented in the balance sheet as a direct reduction in the carrying amount of that debt liability. The amendments in ASU 2015-03 are effective for the annual periods ending after December 15, 2015. The Company adopted the standard retrospectively to all periods presented on the required effective date of January 1, 2016, and its adoption had no impact on the Company's financial position, results of operations or cash flows.

In November 2014, the FASB issued ASU No. 2014-16, *Determining Whether the Host Contract in a Hybrid Financial Instrument Issued in the Form of a Share Is More Akin to Debt or to Equity* ("ASU 2014-16"). The guidance requires an entity to determine the nature of the host contract by considering all stated and implied substantive terms and features of the hybrid financial instrument, weighing each term and feature on the basis of the relevant facts and circumstances (commonly referred to as the whole-instrument approach). The Company adopted the standard retrospectively to all periods presented on the required effective date of January 1, 2016, and its adoption had no impact on the Company's financial position, results of operations or cash flows.

In August 2014, the FASB issued ASU No. 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern(Subtopic 205-40)* ("ASU 2014-15"). The amendments in this update explicitly require a company's management to assess an entity's ability to continue as a going concern and to provide related footnote disclosures in certain circumstances. The new standard is effective in the first annual period ending after December 15, 2016. The Company adopted ASU 2014-15 as of the required effective date of December 31, 2016. This guidance relates to footnote disclosure only (see Note 1), and its adoption had no impact on the Company's financial position, results of operations or cash flows.

## **Recently Issued Accounting Pronouncements**

In October 2016, the FASB issued ASU No. 2016-16, *Income Taxes (Topic 740): Intra-Entity Transfer of Assets Other than Inventory* ("ASU 2016-16"), which requires the recognition of the income tax consequences of an intra-entity transfer of an asset, other than inventory, when the transfer occurs. The standard is effective for annual periods beginning after December 15, 2017, including interim periods within those fiscal years. The Company is currently evaluating the impact that the adoption of ASU 2016-16 will have on its consolidated financial statements.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows: Classification of Certain Cash Receipts and Cash Payments* ("ASU 2016-15"), to address diversity in practice in how certain cash receipts and cash payments are presented and classified in the statement of cash flows. The standard is effective for annual periods beginning after December 15, 2017, including interim periods within those fiscal years. The Company is currently evaluating the impact that the adoption of ASU 2016-15 will have on its consolidated financial statements.

# NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

## 2. Summary of Significant Accounting Policies (Continued)

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. Early adoption is permitted. The Company is currently evaluating the impact that the adoption of ASU 2016-02 will have on its consolidated financial statements.

In May 2014, the FASB issued ASU No. 2014-09, Revenue from Contracts with Customers (Topic 606) ("ASU 2014-09"), which supersedes existing revenue recognition guidance under GAAP. The standard's core principle is that a company will recognize revenue when it transfers promised goods or services to customers in an amount that reflects the consideration to which the Company expects to be entitled in exchange for those goods or services. The standard defines a five-step process to achieve this principle, and will require companies to use more judgment and make more estimates than under the current guidance. The Company expects that these judgments and estimates will include identifying performance obligations in the customer contract, estimating the amount of variable consideration to include in the transaction price and allocating the transaction price to each separate performance obligation. ASU 2014-09 also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts. In August 2015, the FASB issued ASU 2015-14, Revenue from Contracts with Customers (Topic 606): Deferral of the Effective Date, which delays the effective date of ASU 2014-09 such that the standard is effective for public entities for annual periods beginning after December 15, 2017 and for interim periods within those fiscal years. Early adoption of the standard is permitted for annual periods beginning after December 15, 2016. In March 2016, the FASB issued ASU No. 2016-08, Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations ("ASU 2016-08"), which further clarifies the implementation guidance on principal versus agent considerations in ASU 2014-09. In April 2016, the FASB issued ASU No. 2016-10, Revenue from Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing, clarifying the implementation guidance on identifying performance obligations and licensing. Specifically, the amendments in this update reduce the cost and complexity of identifying promised goods or services and improve the guidance for determining whether promises are separately identifiable. The amendments in this update also provide implementation guidance on determining whether an entity's promise to grant a license provides a customer with either a right to use the entity's intellectual property (which is satisfied at a point in time) or a right to access the entity's intellectual property (which is satisfied over time). In May 2016, the FASB issued ASU No. 2016-12, Revenue from Contracts with Customers (Topic 606): Narrow-Scope Improvements and Practical Expedients ("ASU 2016-12"), which clarifies the objective of the collectability criterion, presentation of taxes collected from customers, non-cash consideration, contract modifications at transition, completed contracts at transition and how guidance in ASU 2014-09 is retrospectively applied. ASU 2016-08, ASU 2016-10 and ASU 2016-12 have the same effective dates and transition requirements as ASU 2014-09. The

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

## 2. Summary of Significant Accounting Policies (Continued)

Company is currently evaluating the impact that the adoption that these standards will have on its consolidated financial statements, if and when it generates revenue.

## 3. Fair Value of Financial Assets and Liabilities

The following tables present 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 Measurements as of December 31, 2015 Using:           Level 1         Level 2         Level 3         Total									
	Level 1 Level 2 Level 3 Tot										
Liabilities:											
Derivative liability	<u>\$</u>	_	\$		\$	447	\$	447			
	\$	_	\$		\$	447	\$	447			

		F			urements a 2016 Using	
	Level 1		Le	vel 2	Level 3	Total
Liabilities:						
Warrant liability	\$ -	_	\$		\$ 780	\$ 780
Derivative liability	-	_			512	512
Contingent equity liability	-	_			18,938	18,938
	\$ -	_	\$		\$ 20,230	\$ 20,230

During the years ended December 31, 2015 and 2016, there were no transfers between Level 1, Level 2 and Level 3.

## 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 agreed to issue to the guarantor and co-guarantor of its obligations under a credit agreement (see Note 8). 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 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 future expected share prices, to value the warrant liability. The Monte Carlo simulation incorporated assumptions and estimates to value the warrant liability. Estimates and assumptions impacting the fair value measurement included the estimated probability of adjusting the exercise price of the warrants, 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 Company estimated the fair value per share of its common shares as well as additional factors that the Company deemed relevant. The Company historically has been a private

# NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

## 3. Fair Value of Financial Assets and Liabilities (Continued)

company and 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 the probability-weighted expected return method ("PWERM"), which considered as inputs the type and probability of occurrence of a change-of-control event, the amount of the payment, the expected timing of a change-of-control event and a risk-adjusted discount rate.

## 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 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 July 8, 2016, the assumed probability of occurrence of the event that was most probable of triggering the issuance of shares was 70%, 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%. As of December 31, 2016, the assumed probability of occurrence of the event that was most probable of triggering the issuance of the event that was most probable of triggering the issuance of the event that was most probable of triggering the issuance of the event that was most probable of triggering the issuance 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%. Based on these inputs, the Company determined that the fair value of the contingent equity liability was \$13,125 as of July 8, 2016, the date the Company entered into the license agreement with BMS, and \$14,063 as of December 31, 2016.

*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.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

## 3. Fair Value of Financial Assets and Liabilities (Continued)

The shares related to the first tranche become issuable if the Company completes an equity financing transaction with aggregate proceeds of at least \$30,000 prior to December 31, 2016. As of October 5, 2016, the date the Company entered into the license agreement with AstraZeneca, the Company determined that the fair value of the first tranche contingent equity liability was \$4,500. In determining this fair value, the assumed probability of completing a qualifying equity financing transaction prior to December 31, 2016 was 90%, the expected timing of such event was estimated to be three months, the value of the contingently issuable equity was \$5,000 and the discount rate was assessed to be 0%. 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 liability to fair value, resulting in recognition of other expense of \$500 in the consolidated statement of operations and comprehensive loss in the year ended December 31, 2016. 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 the first tranche contingent equity liability, equal to the then-current fair value of \$5,000, to 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 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 and (ii) any liquidity event, including an initial public offering, any change of control or any assignment of the Company's rights or obligations under the license agreement. As of October 5, 2016, the date the Company entered into the license agreement with AstraZeneca, the Company determined that the fair value of the second tranche contingent equity liability was \$4,050. In determining this fair value, the assumed probability of occurrence of the event that was most probable of triggering the issuance of shares was 60%, the expected timing of such an event was estimated to be less than one year, the value of the contingent equity liability of occurrence of the event that was most probable of triggering that the fair value of the second tranche contingent equity liability of occurrence of the event that was most probable of triggering the issuable equity was \$7,500 and the discount rate was assessed to be 0%. 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%.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

## (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:

	 arrant ability	ivative ability	ontingent ity Liability
Balance at December 31, 2014	\$ _	\$ 77	\$ 
Change in fair value	—	370	
Balance at December 31, 2015		447	
Initial fair value of warrant liability	934		
Initial fair value of contingent equity liability			21,675
Issuance of Series A preferred shares in settlement of first			
tranche of contingent equity liability to AstraZeneca			(5,000)
Change in fair value	(154)	65	2,263
Balance at December 31, 2016	\$ 780	\$ 512	\$ 18,938

# 4. Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following:

	Decen	ıber 31,
	2015	2016
Prepaid clinical trial costs	\$ 387	\$ 388
Other	40	15
	\$ 427	\$ 403

## 5. Equity Method Investment

On August 29, 2016, the Company executed a stock purchase agreement with Kleo Pharmaceuticals, Inc. ("Kleo") to purchase 3,000,000 shares of common stock in 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. Under the terms of the Kleo SPA, the Company committed to purchase 3,000,000 shares upon the initial closing on August 31, 2016, and the remaining 5,500,000 shares are 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 Kleo SPA, the Company agreed to purchase an additional 500,000 shares of Kleo common stock from an officer and stockholder of Kleo. In March 2017, the Company completed the purchase of these shares. The consideration paid for these shares consisted of a cash payment of \$250 and the Company's issuance of 32,500 common shares (see Note 20).

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

# NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

## (Amounts in thousands, except share and per share amounts)

## 5. Equity Method Investment (Continued)

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 the investment date and as of December 31, 2016, and will be performed as of each subsequent reporting date. 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. Based on the outcome of this assessment, the Company concluded that consolidation of Kleo is not appropriate, and has therefore accounted for the investment under the equity method.

The Company's purchase of 3,000,000 shares of Kleo's common stock represented a 21.7% interest and an 18.6% interest in the outstanding shares of Kleo as of August 29, 2016 and December 31, 2016, respectively. In connection with the investment, the Company also received the right to designate two of the five members of Kleo's board of directors. The Company accounts for its investment in Kleo under the equity method of accounting. The Company recorded its initial investment in Kleo based on the \$3,000 cost of the investment. The difference between the cost of the Company's investment in Kleo and its proportionate share of the net assets of Kleo was allocated to goodwill and indefinite-lived intangible assets. The Company will record future adjustments to the carrying value of its investment at each reporting date equal to its proportionate share of Kleo's net income or loss for the corresponding period. The Company recorded other expense of \$247 for the year ended December 31, 2016, and a corresponding reduction in the carrying value of its investment in Kleo at December 31, 2016, for its proportionate share of Kleo's net loss for the period in which the investment was held.

The carrying value of the Company's investment in Kleo was \$2,753 as of December 31, 2016 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, 2016.

Summarized financial information for Kleo was as follows:

Loss from operations

Net loss

	December 31, 2016
Current assets	\$ 4,269
Total assets	\$ 4,317
Current liabilities	\$ 413
Total liabilities	\$ 656
	Year Ended
	December 31, 2016
Revenue	\$ —

F-22

\$

\$

(2,815)

(2,835)

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# BIOHAVEN PHARMACEUTICAL HOLDING COMPANY LTD.

# NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

## 6. Property and Equipment, Net

Property and equipment, net consisted of the following:

	Decem	December 31,		
	2015	20	016	
Computer equipment	\$ 8	\$	34	
Less: Accumulated depreciation	(3)		(8)	
	\$ 5	\$	26	
		-		

Depreciation expense was \$2 and \$5 for the years ended December 31, 2015 and 2016, respectively.

# 7. Accrued Expenses

Accrued expenses consisted of the following:

	December 31,		
	2015	2016	
Accrued clinical trial costs	\$ 104	\$ 2,204	
Accrued professional fees	82	516	
Accrued employee compensation and benefits	9	27	
Accrued income taxes		99	
Other	66	134	
	\$ 261	\$ 2,980	

## 8. Notes Payable

### **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 agreement. Borrowings under the Credit Agreement bear interest at a rate equal to monthly LIBOR plus 1.50% per annum, and the agreement requires monthly, interest-only payments beginning on September 30, 2016 through August 30, 2017 (the "Maturity Date"), when all amounts of unpaid principal and interest become due. The monthly LIBOR rate is reset each month ("LIBOR Period"). As of December 31, 2016, the interest rate applicable to the Loan was 2.27% per annum. In the event of a default, the interest rate applicable is equal to the monthly LIBOR rate then in effect, increased by 4.0% per annum. The Company's obligations under the Credit Agreement are guaranteed by an outside director and shareholder of the Company (the "Guarantor"). A second outside director and shareholder of the Company (the "Guarantor"). A second outside director and shareholder of the Company (the second director agreed to reimburse the Guarantor for one-half of any guaranty obligations that the Guarantor pays to Wells Fargo.

The Credit Agreement also provides that the Company may voluntarily prepay the Loan at any time; however, if the Company elects to prepay the Loan or the Loan otherwise is accelerated and becomes payable prior to the Maturity Date, the Company will pay a prepayment premium, which will be the

# NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

#### 8. Notes Payable (Continued)

additional interest that would have accrued if the Loan remained outstanding through the end of the current monthly LIBOR Period. The Credit Agreement contains affirmative and negative covenants, but does not contain any financial covenants.

The Loan is guaranteed by the Guarantor pursuant to a continuing guaranty agreement entered into between the Guarantor and Wells Fargo. The Guarantor entered into a separate guaranty agreement with another outside director and shareholder of the Company (the "Co-Guarantor"), pursuant to which the Co-Guarantor agreed to reimburse the Guarantor for one half of any guaranty obligations paid by the Guarantor to Wells Fargo.

There were no principal payments due or paid under the Credit Agreement during the year ended December 31, 2016.

In connection with entering into the Credit Agreement on August 30, 2016, the Company agreed to issue warrants to purchase \$1,000 of common shares to each of the Guarantor and Co-Guarantor. The number of common shares issuable upon exercise of each warrant is determined by dividing \$1,000 by the price per share paid by investors in the Series A First Closing (see Note 10). On January 26, 2017, the Company issued the warrants to the Guarantor and Co-Guarantor (see Note 9).

The Company determined that the obligation to issue the warrants represented a liability that was considered outstanding for accounting purposes on August 30, 2016, the date of the Credit Agreement (see Note 9). The fair value of the warrant liability upon issuance represented a premium paid for the guaranty of the Loan, and, accordingly, the Company recorded the issuance-date fair value of the warrant liability of \$934 as a debt discount and as a warrant liability in the Company's consolidated balance sheet. In addition, the Company paid an arrangement fee of \$150 to the lender and incurred legal costs of \$47, both of which were recorded as a debt discount. The debt discount is reflected as a reduction of the carrying value of the notes payable on the Company's consolidated balance sheet and is being amortized to interest expense over the term of the note using the effective interest method.

The Company recognized interest expense of \$385 during the year ended December 31, 2016, including \$347 related to the accretion of the debt discount. As of December 31, 2016, the unamortized debt discount was \$784.

#### Notes Payable to Related Parties

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. The Company funded the acquisition through the issuance of promissory notes to each of the former stockholders of BPI. The former beneficial stockholders of BPI 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. The notes are payable in five annual payments, the first four of which are interest only, with the final payment to include the principal balance outstanding plus any accrued and unpaid interest. The notes bear interest at a rate of 4.5% per annum and mature on December 31, 2021. The notes become 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. There are no affirmative, negative or financial covenants associated with the notes.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

## 8. Notes Payable (Continued)

As of December 31, 2016, the aggregate minimum future principal payments of the Company's debt are summarized as follows:

Year Ending December 31,	
2017	\$ 5,000
2018	
2019	_
2020	_
2021	595
	\$ 5,595

# 9. Warrants

#### **ALS Biopharma Warrants**

On August 10, 2015, as partial consideration issued in connection with a license agreement with ALS Biopharma LLC ("ALS Biopharma") (see Note 13), the Company issued to ALS Biopharma a warrant to purchase 275,000 common shares at an exercise price of \$5.60 per share. The warrant was immediately exercisable upon issuance and expires 10 years from the issuance date. The warrant was classified as equity and recorded at its fair value on the date of issuance, which was estimated to be \$1,231 using the Black-Scholes option-pricing model with the following assumptions: 89.9% volatility; 2.20% risk-free interest rate; 10-year expected term; and no dividend yield. The issuance-date fair value of the warrant was recorded as research and development expense in the consolidated statement of operations and comprehensive loss, and as additional paid-in capital in the consolidated balance sheet.

On August 10, 2015, in connection with the same license agreement, the Company issued to ALS Biopharma a warrant to purchase 325,000 common shares at an exercise price of \$5.60 per share. The warrant became exercisable upon the Company's filing of an investigational new drug application ("IND") for a patented product under the license agreement, and expires 10 years from the issuance date. On May 31, 2016, the Company filed an IND for a patented product under the license agreement. The warrant was classified as equity and recorded at its fair value on May 31, 2016, which was estimated to be \$2,127 using the Black-Scholes option-pricing model with the following assumptions: 85.7% volatility; 1.84% risk-free interest rate; 10-year expected term; and no dividend yield. The issuance-date fair value of the warrant was recorded as research and development expense in the consolidated statement of operations and comprehensive loss, and as additional paid-in capital in the consolidated balance sheet.

#### **Guarantor and Co-Guarantor Warrants**

The Company agreed to issue warrants to purchase \$1,000 of common shares to each of the Guarantor and Co-Guarantor of the Credit Agreement (see Note 8), who are members of the Company's board of directors (see Note 17). The number of common shares issuable upon exercise of each warrant is determined by dividing \$1,000 by the price per share paid by investors in the Series A First Closing (see Note 10). As of December 31, 2016, the warrants had not yet been issued.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

#### 9. Warrants (Continued)

The Company determined that the obligation to issue the warrants represented a liability that was considered outstanding for accounting purposes on August 30, 2016, the date the Company entered into the Credit Agreement. 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 Company's consolidated statement of operations and comprehensive loss. Changes in the fair value of the warrant liability will continue to be recognized until the warrants are exercised, expire or qualify for equity classification.

The fair value of the warrant liability was determined to be \$934 on the date of issuance. The Company remeasured the liability as of December 31, 2016 and determined that the fair value of the warrant liability was \$780, resulting in a gain of \$154 recorded within other income (expense), net in the consolidated statements of operations for the year ended December 31, 2016.

On January 26, 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. The warrants were immediately exercisable and expire upon the earlier to occur of (i) the fifth anniversary of the issuance date of the warrants and (ii) the second anniversary of the Company's initial public offering. Upon issuance, the Company continued to classify these warrants as a liability on the consolidated balance sheet because the warrants contain anti-dilution price protection provisions through January 26, 2018. As a result, changes in the fair value of the warrant liability will continue to be recognized as a component of other income (expense), net until the earliest of (i) the exercise of the warrants, (ii) the expiration of the warrants or (iii) January 26, 2018.

#### **10. Convertible Preferred Shares**

As of December 31, 2016, the Company's memorandum and articles of association, as amended and restated, authorized the Company to issue 11,242,172 Series A preferred shares. The holders of Series A preferred shares have liquidation rights in the event of a deemed liquidation that, in certain situations, is not solely within the control of the Company. Therefore, the Series A preferred shares are classified outside of shareholders' equity (deficit).

In October 2016, the Company issued and sold an aggregate of 4,305,209 Series A preferred shares, at an issuance price of \$9.2911 per share, for proceeds of \$37,295, net of offering costs of \$2,705 (the "Series A First Closing"). The \$2,705 of offering costs consisted of \$1,730 payable in cash and 105,010 shares of the Company's Series A preferred shares valued at \$975, or \$9.2911 per share. The preferred share purchase agreement provides for the issuance of additional Series A preferred shares in a second and final tranche (the "Series A Second Closing"). The Series A Second Closing was contingent upon the results of the Company's oral contraceptive drug-drug interaction study for rimegepant. One of the investors was designated to review the results of the study and within 21 days notify the Company if it elected to proceed with the Series A Second Closing. The Company determined that the future tranche obligation did not meet the definition of a freestanding financial instrument because, while separately exercisable, it was not legally detachable. Further, the Company determined that the embedded future

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

## (Amounts in thousands, except share and per share amounts)

#### **10. Convertible Preferred Shares (Continued)**

tranche obligation did not meet the definition of a derivative, which would require bifurcation for accounting purposes, as it does not provide for net settlement.

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 at an issuance price of \$9.2911 per share for net cash proceeds of \$38,635 (see Note 20). The offering costs for the second tranche consisted of \$1,365 payable in cash and 105,009 shares of the Company's Series A preferred shares.

In October 2016, 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 contingently issuable equity under the Company's license agreement with AstraZeneca (see Note 13).

The holders of the Series A preferred shares have the following rights and preferences:

#### Voting

The holders of Series A preferred shares are entitled to vote, together with the holders of common shares, on all matters submitted to shareholders for a vote. The holders of Series A preferred shares are entitled to the number of votes equal to the number of common shares into which their Series A preferred shares could convert.

#### **Conversion**

Each Series A preferred share is convertible into common shares at the option of the shareholder at any time after the date of issuance. In addition, each Series A preferred share will be automatically converted into common shares, at the applicable conversion ratio then in effect, upon the earlier of (i) a firm commitment public offering with proceeds to the Company of at least \$50,000, before deducting underwriting discounts and commissions or (ii) the date specified by the vote or written consent of the holders of a majority of the then outstanding Series A preferred shares.

The conversion ratio of Series A preferred shares is determined by dividing the Original Issue Price by the Conversion Price. The Original Issue Price of the Series A preferred shares is \$9.2911 per share. The Conversion Price of the Series A preferred shares is \$9.2911 per share, subject to appropriate adjustment in the event of any stock split, stock dividend, combination or other similar recapitalization and other adjustments as set forth in the Company's memorandum and articles of association, as amended and restated. On the date of issuance, each Series A preferred share is convertible into one common share. In the event that any Series A preferred stock investor does not participate in the second and final tranche of the Series A preferred financing, that investor's shares will be convertible into common shares at a ratio of one common share for every 1,000 Series A preferred shares. In addition, if the Company decides not to move forward with a Phase 3 clinical trial on its product candidate, rimegepant, or if the Company fails to initiate a Phase 3 clinical trial prior to October 1, 2017, the Conversion Price of the Series A preferred shares will be reduced to \$7.0613 per share.

### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

### **10. Convertible Preferred Shares (Continued)**

#### **Dividends**

The holders of Series A preferred shares are entitled to receive dividends in preference to any dividend on common shares at the rate of 8.0% per year of the Original Issue Price. Dividends shall accrue daily and compound annually, whether or not declared, shall be payable when, as and if declared by the board or directors of the Company and shall be noncumulative. The Company may not declare, pay or set aside any dividends on shares of any other class or series of capital stock of the Company unless the holders of Series A preferred shares then outstanding first receive, or simultaneously receive, dividends on each outstanding Series A preferred share.

Accruing dividends, whether or not declared, shall be payable upon any liquidation event. Declared but unpaid dividends are payable upon the conversion of the Series A preferred shares into common shares.

#### Liquidation

In the event of any voluntary or involuntary liquidation, dissolution or winding-up of the Company or a Deemed Liquidation Event (as described below), the holders of Series A preferred shares then outstanding will receive, in preference to holders of common shares, an amount equal to the greater of (i) the Original Issue Price per share, plus all dividends declared but unpaid on such shares or (ii) the amount such holders would have received had all of their Series A preferred shares been converted into common shares immediately prior to such liquidation event. If upon any such liquidation event, the assets of the Company available for distribution are insufficient to permit payment in full to the holders of Series A preferred shares, the proceeds will be ratably distributed among the holders of Series A preferred shares in proportion to the respective amounts that they would have received if they were paid in full.

After payments have been made in full to the holders of Series A preferred shares, the remaining assets of the Company available for distribution shall be distributed among the holders of common shares ratably in proportion to the number of shares held by each such holder.

Unless a majority of the holders of the then outstanding Series A preferred shares elect otherwise, a Deemed Liquidation Event shall include a merger or consolidation (other than one in which shareholders of the Company own a majority by voting power of the outstanding shares of the surviving or acquiring corporation) or a sale, lease, transfer, exclusive license or other disposition of all or substantially all of the assets of the Company.

#### **Redemption**

The Company's memorandum and articles of association, as amended and restated, does not provide redemption rights to the holders of Series A preferred shares.

### **11. Common Shares**

As of December 31, 2015 and 2016, the Company's memorandum and articles of association, as amended and restated, authorized the Company to issue 17,500,000 shares and 38,000,000 shares, respectively, of no par value common shares.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

### (Amounts in thousands, except share and per share amounts)

#### 11. Common Shares (Continued)

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, if any. Through December 31, 2016, no dividends have been declared.

In September 2013, the Company issued 250,000 common shares to Yale in connection with a license agreement (see Note 13). Also in September 2013, the Company issued 3,350,000 common shares to Company founders and inventors and 1,300,000 common shares to the Chairman of the Company's board of directors and co-founder of BPI.

In January 2014, the Company issued 5,752,000 common shares at an issuance price of \$0.61 per share for proceeds of \$3,435, net of issuance costs of \$65. Pursuant to the terms of the securities purchase agreement, the purchase price for the common shares was payable in four installments, with \$1,750 due at closing, \$750 due on August 1, 2014, \$500 due on December 3, 2014 and \$500 due on February 4, 2015. As of December 31, 2014, the Company reported a note receivable from shareholder for the final installment of \$500 on its consolidated balance sheet. The investor paid the final installment of \$500 in 2015.

In July 2015, the Company issued 867,000 common shares at an issuance price of \$5.60 per share for proceeds of \$4,816, net of issuance costs of \$37.

In August 2015, the Company issued 50,000 common shares valued at \$262 in partial settlement of consideration due under a license agreement.

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. Upon CII's exercise of the Put Option, the Company would be obligated to purchase CII's shares for a price that is the greater of (i) the current market price of such share and (ii) the original purchase price of such share. The right to put the shares will terminate at such time that the shares may be sold (i) pursuant to an effective registration statement under the Securities Act of 1933 (the "Securities Act"), (ii) pursuant to Rule 144 promulgated under the Securities Act, but in each case, only after the termination of any applicable "lock-up" restrictions and, in the case of (ii), only if the common shares are then listed for trading on a national securities exchange. The fair value of the Put Option was determined to be \$0 upon execution of the agreement and as of December 31, 2016 because the ability to maintain a presence in Connecticut is within the Company's control.

# NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

#### 12. Share-Based Compensation

#### 2014 Equity Incentive Plan

The Company's 2014 Equity Incentive Plan, as amended, (the "2014 Plan") provides 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 2014 Plan is administered by the board of directors, or at the discretion of the board of directors, by a committee of the board. 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 ten years.

The total number of common shares that may be issued under the 2014 Plan was 4,000,000 shares as of December 31, 2015. 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. As of December 31, 2016, 1,034,805 shares remained available for future grant under the 2014 Plan.

Vesting periods are determined at the discretion of the board of directors. Stock options granted to employees and directors typically vest over three years. Stock options granted to non-employees typically vest over three years. The Company measures and records the value of these options over the period of time services are provided and, as such, unvested portions are subject to remeasurement at subsequent reporting periods.

During the years ended December 31, 2015 and 2016, the Company granted options to purchase 637,500 common shares and 417,875 common shares, respectively, to employees and directors. The Company recorded share-based compensation expense for options granted to employees and directors of \$1,137 and \$2,284 during the years ended December 31, 2015 and 2016, respectively.

During the years ended December 31, 2015 and 2016, the Company granted options to purchase 610,000 common shares and 199,050 common shares, respectively, to non-employees. The Company recorded share-based compensation expense for options granted to non-employees of \$1,700 and \$2,319 during the years ended December 31, 2015 and 2016, respectively.

### **Stock Option Valuation**

The assumptions that the Company used to determine the grant-date fair value of stock options granted to employees and directors were as follows, presented on a weighted average basis:

	Year Ended December 31,
	2015 2016
Risk-free interest rate	1.62% 2.19%
Expected term (in years)	5.75 5.75
Expected volatility	58.51% 70.58%
Expected dividend yield	0% 0%
Exercise price	\$ 5.60 \$ 9.29
Fair value of common share	\$ 5.23 \$ 6.73

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

## (Amounts in thousands, except share and per share amounts)

#### 12. Share-Based Compensation (Continued)

The assumptions that the Company used to determine the grant-date fair value of stock options granted to non-employees were as follows, presented on a weighted average basis:

	Year Ended December 31,	
	2015 2016	
Risk-free interest rate	2.09% 2.549	6
Expected term (in years)	10.0 10.0	
Expected volatility	61.61% 67.16%	6
Expected dividend yield	0% 0%	6
Exercise price	\$ 5.60 \$ 9.29	
Fair value of common share	\$ 5.23 \$ 6.73	

# Stock Options

Stock option activity under the 2014 Plan is summarized as follows:

	Number of Shares	A E	eighted verage xercise Price	Weighted Average Remaining Contractual Term		ggregate ntrinsic Value
Outstanding as of December 31, 2015 Granted	3,247,500 616,925	\$ \$	2.53 9.29	(in years) 9.68	\$	9,983
Exercised Forfeited	_		_			
Outstanding as of December 31, 2016	3,864,425	\$	3.61	9.21	\$	15,991
Options exercisable as of December 31, 2016 Options unvested as of December 31, 2016	2,277,981 1,586,444	\$ \$	2.56 5.10	8.30 8.87	\$ \$	11,416 4,575

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. There have been no exercises as of December 31, 2016.

The weighted average grant-date fair value per share of stock options granted during the years ended December 31, 2015 and 2016 was \$3.22 and \$4.09, respectively.

The total fair value of options vested during the years ended December 31, 2015 and 2016 was \$2,345 and \$3,381, respectively.

### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

#### 12. Share-Based Compensation (Continued)

#### **Share-Based Compensation**

Share-based compensation expense was classified in the consolidated statements of operations and comprehensive loss as follows:

	Year Decem	Ended ber 31,
	2015	2016
Research and development expense	\$ 1,527	\$ 2,382
General and administrative expense	1,310	2,221
	\$ 2,837	\$ 4,603

As of December 31, 2016, total unrecognized compensation cost related to the unvested share-based awards was \$5,258, which is expected to be recognized over a weighted average period of 1.53 years.

#### **13. License 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 the event that Yale's fully diluted ownership position following the closing of the Company's first two financings with institutional investors resulting in an investment of at least \$3,500 fell below 1% of the Company's fully diluted common shares outstanding, the Company would be required to issue to Yale an additional number of shares of common shares such that Yale's ownership position is restored to no less than 1%. The obligation to contingently issue equity to Yale was determined to be a liability, which was accounted for at fair value and remeasured at each reporting date. The fair value of the obligation at inception of the Yale's ownership percentage below 1% was remote. The fair value of the liability remained at \$0 through the completion of the Company's common share issuances in January 2014 and July 2015, at which time the contingent obligation terminated, as Yale's ownership position remained above 1%.

The Yale Agreement provides for a change-of-control payment to Yale upon the occurrence of a change-of-control event, as defined in the agreement, including an initial public offering. Upon the occurrence of a change-of-control event, the Company is 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 and (ii) \$1,500. If the change-of-control event is as an initial public offering, the amount the Company will be obligated to pay to Yale will be reduced by the value of Yale's equity investment in the Company on the first day that Yale is free to sell its equity interest. The Company classifies the change-of-control payment obligation as a liability on its consolidated balance sheet because it represents 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

### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

### (Amounts in thousands, except share and per share amounts)

#### 13. License Agreements (Continued)

fair value of the derivative liability of \$14 was recognized as research and development expense in the consolidated statement of operations and comprehensive loss upon entering into the agreement with Yale. The derivative liability is remeasured to fair value at each reporting date. Changes in the fair value of the derivative 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 derivative liability will continue to be recognized until a change-of-control event occurs.

For the years ended December 31, 2015 and 2016, the Company recorded other expense of \$370 and \$65, respectively, for the change in the fair value of the derivative liability. The fair value of the derivative liability was \$447 and \$512 as of December 31, 2015 and 2016, respectively.

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.

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. The Company also agreed to reimburse Yale for its past costs related to the licensed patents, which were estimated to be \$18 in the aggregate. 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 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.

The Company recorded research and development expenses of \$84 and \$4 for the years ended December 31, 2015 and 2016 for reimbursement of patent fees in connection with the Yale Agreement.

#### **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. Under the MGH Agreement, the Company paid MGH an upfront license fee of \$20. The Company is also obligated to pay MGH annual license maintenance fees of between \$30 and \$50, beginning in 2017, 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

# NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

## (Amounts in thousands, except share and per share amounts)

#### 13. License Agreements (Continued)

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.

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 Company also agreed to reimburse MGH for its past costs related to the licensed patents, which were estimated to be \$13 in the aggregate. The MGH Agreement expires upon expiration of the patent rights under the MGH Agreement, unless earlier terminated by either party.

The Company did not recognize any research and development expense associated with the MGH Agreement during the years ended December 31, 2015 and 2016.

### **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 trigriluzole, 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 paid ALS Biopharma \$1,000 upon entering into the agreement as well as additional payments of \$500 and \$1,000 during the years ended December 31, 2015 and 2016, respectively, which amounts represented funding for research to be performed by ALS Biopharma in connection with a mutually agreed upon research plan. The Company is also 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 a swell as royalty payments of a low single-digit percentage based on net sales of products licensed under the agreement, payable on a quarterly basis.

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 will become exercisable upon the Company's achievement of a specified regulatory milestone (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.

### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

## (Amounts in thousands, except share and per share amounts)

#### 13. License Agreements (Continued)

The Company recorded research and development expenses of \$2,836 and \$3,127 for the years ended December 31, 2015 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, as well as the upfront payments made at the time of signing the ALS Biopharma Agreement.

#### **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 in the aggregate of \$75 for the first five years following execution of the agreement, then \$25 per year thereafter until the first commercial sale of a licensed product, at which point the Company will pay Rutgers minimum annual royalties totaling in the low six-digits. The Company is also obligated 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 0.3% 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 because it represents 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 fair value of the obligation upon execution of the Rutgers Agreement 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 fair value of the liability remained at \$0 through December 31, 2016.

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 Company also agreed to reimburse Rutgers for its past costs related to the licensed patent, which were estimated to be \$72. 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.

The Company recorded research and development expense of \$72 for the year ended December 31, 2016, which consisted of the reimbursed patent fees.

### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

### (Amounts in thousands, except share and per share amounts)

#### 13. License Agreements (Continued)

#### **BMS** Agreement

In July 2016, the Company entered into an exclusive, worldwide license agreement (the "BMS Agreement") with BMS 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 made upfront payments to BMS totaling \$9,000 during the year ended December 31, 2016 in connection with the BMS 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 \$150,000 for each licensed product upon the achievement of commercial milestones. In addition, the Company is obligated to pay up to \$150,000 for each licensed product upon the achievement 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 for completing the financing transaction to October 31, 2016, on which date the Series A First Closing was completed (see Note 10).

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 initial public offering or

# NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

## (Amounts in thousands, except share and per share amounts)

#### 13. License Agreements (Continued)

(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 10), 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 as of December 31, 2016 and recognized expense of \$938 for the increase in the fair value of the liability to \$14,063. Changes in the fair value of the contingent equity 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 contingent equity liability will continue to be recognized until the occurrence of a triggering event.

The Company recorded research and development expense of \$22,125 related to the BMS Agreement for the year ended December 31, 2016, which consisted of \$13,125 for the issuance-date fair value of the contingent equity liability and \$9,000 for the upfront license payments made to BMS.

#### AstraZeneca Agreement

In October 2016, the Company entered into an exclusive license agreement (the "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, 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 Company made an upfront payment of \$5,000 during the year ended December 31, 2016. 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 of mid single-digit to low double-digit percentages. If the Company receives revenue from sublicensing any of its rights under the AstraZeneca Agreement, the Company is also obligated to pay a portion of that revenue to AstraZeneca. 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 AstraZeneca Agreement.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

#### 13. License Agreements (Continued)

The 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 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 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 initial public offering of the Company, any change of control of the Company or any assignment of the Company's rights and obligations under the 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 10). 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.

The obligations to contingently issue equity to AstraZeneca are classified as liabilities on the consolidated balance sheet because they represent obligations to issue a variable number of shares for a fixed dollar amount. Upon entering into the AstraZeneca Agreement, the issuance-date fair values of the First Tranche and Second Tranche contingent equity liabilities of \$4,500 and \$4,050, respectively, were recognized as research and development expense in the consolidated statement of operations and comprehensive loss. Changes in the fair value of the contingent equity liabilities 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 contingent equity liabilities will continue to be recognized until the occurrence of a respective triggering event.

In October 2016, upon completion of the Series A First Closing (see Note 10), 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. Immediately prior to the completion of the Series A First Closing, the Company remeasured the contingent equity liability associated with the First Tranche to fair value, resulting in recognition of other expense of \$500. 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.

As of December 31, 2016, the Company determined that the fair value of the contingent equity liability associated with the Second Tranche was \$4,875, which resulted in the recognition of other expense of \$825 during the year ended December 31, 2016.

### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

### (Amounts in thousands, except share and per share amounts)

#### 13. License Agreements (Continued)

The Company recorded research and development expense of \$13,550 related to the AstraZeneca Agreement for the year ended December 31, 2016, which consisted of \$8,550 for the issuance-date fair value of the contingent equity liability and \$5,000 for the upfront license fee paid to AstraZeneca.

#### Agreement with Catalent

In March 2015, the Company entered into a development and license agreement with Catalent U.K. Swindon Zydis Limited ("Catalent") pursuant to which the Company obtained license rights to the Zydis technology in BHV-0223. BHV-0223 was developed under this agreement, and Catalent has manufactured BHV-0223 for clinical testing. The Company made an upfront payment of \$275 to Catalent upon entering into the agreement and is obligated to pay Catalent up to \$1,575 upon the achievement of specified regulatory and commercial milestones. The Company is 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, the Company is responsible for conducting clinical trials and for preparing and filing regulatory submissions. The Company has the right to sublicense its rights under the Catalent 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 the Company. 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 the Company fails to meet specified development timelines, which it may extend in certain circumstances.

The Company recorded research and development expense of \$275 for the year ended December 31, 2015 under the agreement with Catalent, consisting of the upfront license fee. The Company did not record any research and development expense related to the agreement during the year ended December 31, 2016.

# 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.

In addition, in each reporting period, the Company's tax provision includes the effects of consolidating the results of operations of BPI, either through December 30, 2016 as a variable interest entity or as of December 31, 2016 as the Company's wholly owned subsidiary. BPI is subject to taxation in the United States. 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

**Vear Ended** 

### **BIOHAVEN PHARMACEUTICAL HOLDING COMPANY LTD.**

### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

#### (Amounts in thousands, except share and per share amounts)

#### 14. Income Taxes (Continued)

carryforwards for all periods through September 30, 2016. BPI's U.S. net operating loss carryforwards are reflected as foreign net operating loss carryforwards in the following discussion.

During the three months ended December 31, 2016, the Company fully utilized BPI's remaining U.S. net operating loss carryforwards due to BPI's profitability in that period and the Company recorded a full release of the valuation allowance of \$9 due to management's reassessment of the amount of deferred tax assets that it believes are more likely than not to be realized. As a result, the Company recorded an income tax provision for the first time during the three months ended December 31, 2016.

Income (loss) before provision for income taxes consisted of the following:

	Decemb	
	2015	2016
BVI	\$ (10,062)	\$ (63,677)
Foreign (U.S.)	(4)	233
Loss before provision for income taxes	\$ (10,066)	\$ (63,444)

The provision for income taxes consisted of the following:

	Year I Decem	
	2015	2016
Current income tax provision:		
BVI	\$ —	\$ —
Foreign (U.S. federal and state)		99
Total current income tax provision		99
Deferred income tax provision (benefit):		
BVI		_
Foreign (U.S. federal and state)		(9)
Total deferred income tax provision (benefit)		(9)
Total provision for income taxes	\$	\$ 90

A reconciliation of the BVI statutory income tax rate of 0% to the Company's effective income tax rate is as follows:

	Year En Decembe	
	2015	2016
BVI statutory income tax rate	(0.0)%	(0.0)%
Foreign tax rate differential	(0.0)	0.1
Change in valuation allowance	0.0	(0.0)
Effective income tax rate	0.0%	0.1%

# NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

### 14. Income Taxes (Continued)

Net deferred tax assets consisted of the following:

	Decem	ber 31,
	2015	2016
Deferred tax assets:		
Foreign net operating loss carryforwards	\$ 13	\$ —
Other	3	9
Total deferred tax assets	16	9
Valuation allowance	(16)	
Net deferred tax assets	\$	\$ 9

As of December 31, 2016, the Company had no remaining foreign net operating loss carryforwards.

Each reporting period, the Company evaluates the positive and negative evidence bearing on its ability to realize its deferred tax assets.

As of December 31, 2015 and September 30, 2016 (unaudited), BPI's deferred tax assets consisted primarily of its U.S. net operating loss carryforwards. A full valuation allowance had been recorded against BPI's deferred tax assets through September 30, 2016. During the three months ended December 31, 2016, the Company fully utilized BPI's remaining U.S. net operating loss carryforwards and recorded a valuation allowance release of \$9 due to management's reassessment of the amount of deferred tax assets that it believes are more likely than not to be realized.

As of December 31, 2016, the Company released the deferred tax asset valuation allowance in full primarily as a result of BPI achieving three years of cumulative pre-tax income in the U.S. during the three months ended December 31, 2016. In addition, management had determined that sufficient positive evidence existed as of December 31, 2016 to conclude that it is more likely than not that BPI's deferred tax assets are realizable.

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2015 and 2016 were due primarily to the utilization of U.S. net operating loss carryforwards and were as follows:

	j	December 31,		
	20	2015 2016		016
Valuation allowance as of beginning of year	\$	21	\$	16
Decreases recorded as benefit to income tax provision		(5)		(16)
Increases recorded to income tax provision				—
Valuation allowance as of end of year	\$	16	\$	

The Company has not recorded any amounts for unrecognized tax benefits as of December 31, 2015 or 2016. 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, 2015 and 2016, 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 years ended December 31, 2013 and subsequent years. There are currently no income tax examinations pending.

### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

#### 15. Net Loss per Share and Unaudited Pro Forma Net Loss per Share

#### Net Loss per Share Attributable to Common Shareholders of Biohaven Pharmaceutical Holding Company Ltd.

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,			
		2015		2016
Numerator:				
Net loss	\$	(10,066)	\$	(63,534)
Less: Net income (loss) attributable to non-controlling interests		(4)		143
Net loss attributable to common shareholders of Biohaven				
Pharmaceutical Holding Company Ltd.	\$	(10,062)	\$	(63,677)
Denominator:				
Weighted average common shares outstanding-basic and diluted	1	1,009,277		12,608,366
Net loss per share attributable to common shareholders of Biohaven			_	
Pharmaceutical Holding Company Ltd.—basic and diluted	\$	(0.91)	\$	(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 of Biohaven Pharmaceutical Holding Company Ltd. is the same. The Company excluded the following potential common shares, 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,		
	2015	2016		
Options to purchase common shares	3,247,500	3,864,425		
Warrants to purchase common shares	275,000	600,000		
	3,522,500	4,464,425		

In addition to the potentially dilutive securities noted above, as of December 31, 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 8). As of December 31, 2016, the warrants had not yet been issued. Accordingly, the Company has excluded these warrants from the table above and the calculation of diluted net loss per share for the year ended December 31, 2016.

The Company has 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 Note 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.

### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

#### 15. Net Loss per Share and Unaudited Pro Forma Net Loss per Share (Continued)

#### Unaudited Pro Forma Net Loss per Share Attributable to Common Shareholders of Biohaven Pharmaceutical Holding Company Ltd.

The unaudited pro forma basic and diluted net loss per share attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd. for the year ended December 31, 2016 have been prepared to give effect to adjustments arising upon the closing of a qualified initial public offering.

The unaudited pro forma basic and diluted weighted average common shares outstanding used in the calculation of unaudited pro forma basic and diluted net loss per share attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd. for the year ended December 31, 2016 have been prepared to give effect, upon a qualified initial public offering, to the automatic conversion of all outstanding convertible preferred shares into 4,948,369 common shares and the issuance of 1,883,523 common shares to AstraZeneca and BMS pursuant to the Company's license agreements with AstraZeneca and BMS (see Note 13) as if the proposed initial public offering had occurred on the latest of January 1, 2016, the issuance date of the convertible preferred shares or the date the Company entered into each respective license agreement.

Unaudited pro forma 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, 2016 (unaudited)	
Numerator:		
Net loss attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd.	\$ (63,677)	
Denominator:		
Weighted average common shares outstanding—basic and diluted	12,608,366	
Pro forma adjustment to reflect assumed automatic conversion of Series A preferred shares upon the closing of the proposed initial public offering Pro forma adjustment to reflect issuance of shares to AstraZeneca and BMS upon the	824,729	
closing of the proposed initial public offering	782,228	
Pro forma weighted average common shares outstanding-basic and diluted	14,215,323	
Pro forma net loss per share attributable to common shareholders of Biohaven Pharmaceutical Holding Company Ltd.—basic and diluted	\$ (4.48)	

#### **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 expires in October 2018, and the Company has the option to extend the term through October 2021. The agreement requires future minimum lease payments for the years ending December 31, 2017 and 2018 of \$40 and \$35, respectively, totaling \$75.

### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

#### 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 noncontingent payments (see Note 13).

## **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, 2015 and 2016, the Company had committed to minimum payments under these arrangements totaling \$630 and \$6,973, respectively.

#### **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. To date, the Company has not incurred any material costs as a result of such indemnifications. 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, 2015 or 2016.

#### Legal Proceedings

The Company is not a party to any litigation and does not have contingency reserves established for any litigation liabilities.

#### **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, 2015 and 2016, the Company made payments to Yale under the Yale Agreement of \$84 and \$4, respectively. During the years ended December 31, 2015 and 2016, the Company recognized research and development expense under the Yale Agreement of \$84 and \$4, respectively. As of December 31, 2015 and 2016, the Company owed no amounts to Yale.

#### **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 agreed to issue warrants to

### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

## (Amounts in thousands, except share and per share amounts)

#### **17. Related Party Transactions (Continued)**

purchase \$1,000 of common shares to each of the Guarantor and Co-Guarantor in exchange for their respective guaranties (see Notes 8 and 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.

On August 29, 2016, the Company executed a stock purchase agreement with Kleo to purchase 3,000,000 shares of Kleo common stock at a purchase price of \$1.00 per share in an initial closing, which was completed on August 31, 2016, and committed to purchase an aggregate 5,500,000 additional shares of Kleo common stock at a purchase price of \$1.00 per share (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 outside director of the Company. Also, the Chief Executive Officer and controlling stockholder of Kleo is a shareholder of the Company. In addition to the purchases under the stock purchase agreement described above, on August 29, 2016, the Company entered into an agreement with the Chief Executive Officer of Kleo to purchase 500,000 shares 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, 2016, the Company had not performed any services or received any payments under this agreement.

#### **Biohaven Pharmaceuticals, Inc.**

BPI is a related party because its 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. Since the Company's incorporation in September 2013, the Company is deemed to have had a variable interest in BPI, and BPI is deemed to have been a VIE, of which the Company is the primary beneficiary. Accordingly, the Company has consolidated the results of BPI since September 2013. All transactions between the Company and BPI have been eliminated in consolidation. 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.

#### 18. Acquisition of Biohaven Pharmaceuticals, Inc.

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. Prior to the acquisition, the Company was deemed to have had a variable interest in BPI, and BPI was deemed to be a VIE of which the Company was the primary beneficiary. As a result, the Company has consolidated the results of BPI since the Company's incorporation in September 2013, and, prior to the acquisition of BPI, recognized a non-controlling interest in its consolidated balance sheet representing 100% of the capital stock of BPI not owned by the Company. The three founders of BPI, each of whom beneficially owned one-third of the equity of BPI, also serve as the Company's Chairman of the board of directors, Chief Executive Officer, and Chief Medical Officer, respectively (see Note 17).

# NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

#### **18.** Acquisition of Biohaven Pharmaceuticals, Inc. (Continued)

The Company funded the acquisition through the issuance of promissory notes to each of the former stockholders of BPI. The notes are payable in five annual payments, the first four of which are interest only, with the final payment to include the principal balance outstanding plus any accrued and unpaid interest. The notes bear interest at a rate of 4.5% per annum and mature on December 31, 2021. The notes become immediately due and payable upon specified events, including immediately prior to the consummation of the initial public offering of the Company's common shares or upon the occurrence of a change of control of the Company. There are no affirmative, negative or financial covenants associated with the notes.

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.

#### 19. 401(k) Savings Plan

The Company established a defined contribution savings plan under Section 401(k) of the Internal Revenue Code. This plan covers substantially all employees who meet minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pre-tax basis. Company contributions to the plan may be made at the discretion of the Company's board of directors. The Company made no contributions to the plan during the year ended December 31, 2015. During the year ended December 31, 2016, the Company made contributions totaling \$25 to the plan.

#### **20. Subsequent Events**

For its consolidated financial statements as of December 31, 2016 and for the year then ended, the Company evaluated subsequent events through April 3, 2017, the date on which those financial statements were issued.

#### Sale of Series A Preferred Shares

In February 2017, the Company closed the second and final tranche of its Series A preferred financing through the issuance and sale of an aggregate of 4,305,182 Series A preferred shares, at an issuance price of \$9.2911 per share, for net cash proceeds of \$38,635. The offering costs for the second tranche consisted of \$1,365 payable in cash and 105,009 shares of the Company's Series A preferred shares.

## **Purchases of Kleo Common Stock**

On March 30, 2017, the Company purchased 1,375,000 shares of Kleo common stock for cash consideration of \$1,375 pursuant to its commitment under the Kleo SPA (see Note 5).

On March 30, 2017, the Company purchased 500,000 shares of Kleo common stock from the Chief Executive Officer of Kleo pursuant to an agreement dated August 29, 2016. The consideration paid for these shares consisted of a cash payment of \$250 and the Company's issuance of 32,500 common shares.

### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

# (Amounts in thousands, except share and per share amounts)

### **21. Subsequent Events (Unaudited)**

#### **Increase in Authorized Common Shares**

On April 21, 2017, the Company effected an increase in the number of authorized common shares from 38,000,000 shares to 50,000,000 shares.

# 2017 Equity Incentive Plan

On May 3, 2017, the Company's shareholders approved the 2017 Equity Incentive Plan (the "2017 Plan"), which will become effective on the date of execution of the underwriting agreement in connection with the Company's initial public offering. 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. The number of common shares initially reserved for issuance under the 2017 Plan is 7,611,971 shares, which is the sum of (i) 2,712,741 shares, (ii) the number of shares remaining available for issuance under the 2014 Plan and (iii) the number of common shares subject to outstanding awards under the 2014 Plan that expire or terminate for any reason prior to exercise or settlement; are forfeited because of the failure to meet a contingency or condition required to vest such shares or otherwise return to the Company; or are reacquired or withheld (or not issued) to satisfy a tax withholding obligation in connection with an award or to satisfy the exercise price of an award. The number of common shares that may be issued under the 2017 Plan may be increased by the Company's board of directors on January 1 of each year, beginning on January 1, 2018 and continuing through and including January 1, 2027, by a number of common shares determined by the Company's board of directors in an amount not to exceed 4% of the total number of common shares outstanding on December 31 of the preceding calendar year. The common shares underlying any awards that expire or are otherwise terminated, are settled in cash, are repurchased by the Company, or are reacquired in satisfaction of tax withholding obligations or as consideration for the exercise price of an award under the 2017 Plan will be added back to the common shares available for issuance under the 2017 Plan.

#### 2017 Employee Share Purchase Plan

On May 3, 2017, the Company's shareholders approved the 2017 Employee Share Purchase Plan (the "2017 ESPP"), which will become effective on the date of execution of the underwriting agreement in connection with the Company's initial public offering. A total of 339,139 common shares were initially reserved for issuance under this plan. The number of common shares that may be issued under the 2017 ESPP will automatically increase on January 1 of each year, beginning on January 1, 2018 and continuing through and including January 1, 2027, by the least of (i) 600,000 common shares, (ii) 1% of the total number of common shares outstanding on December 31 of the preceding calendar year and (iii) a number of shares determined by the Company's board of directors.

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