2018 Annual Report

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2018

OR

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

Commission File Number 001-37718

Spring Bank Pharmaceuticals, Inc.
(Exact name of Registrant as specified in its charter)

Delaware	**52-2386345**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
35 Parkwood Drive Hopkinton, MA	**01748**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (508) 473-5993

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

Common Stock, $0.0001 par value per share	**The Nasdaq Stock Market LLC (Nasdaq Capital Market)**
(Title of each class)	**(Name of each exchange on which registered)**

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

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

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

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

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). YES ☒ NO ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

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

Large accelerated filer	☐	Accelerated filer	☒
Non-accelerated filer	☐	Smaller reporting company	☒
Emerging growth company	☒		

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the closing price of the shares of common stock on The Nasdaq Stock Market on June 29, 2018, was approximately $128.9 million.

The number of shares of the registrant's Common Stock outstanding as of March 7, 2019 was 16,436,895.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the information required by Part III of Form 10-K will appear in the registrant's definitive proxy statement on Schedule 14A for the 2019 annual meeting of stockholders and are hereby incorporated by reference into this report.

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Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. In some cases, forward-looking statements are identified by the words "anticipate," "believe," "continue," "could," "estimate," "expect," "future," "goals," "intend," "likely," "may," "might," "ongoing," "objective," "plan," "potential," "predict," "project," "seeks," "should," "strategy," "target," "will" and "would" or the negative of these terms, or other comparable terminology intended to identify statements about the future. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Annual Report on Form 10-K, such statements are based on a combination of facts and factors currently known by us and our expectations of the future, about which we cannot be certain. Forward-looking statements include statements about:

- the design, success, cost and timing of our product development activities and future clinical trials;
- our estimates regarding future expenses and needs for additional financing and our estimates regarding our research and development goals;
- our financial performance and our ability to fund our operations and working capital requirements;
- the timing of and our ability to obtain and maintain regulatory approvals for any of our product candidates;
- whether our product candidates will satisfactorily demonstrate safety and efficacy to the FDA and other comparable regulatory organizations;
- our analysis of top line results and other data derived from our clinical and pre-clinical trials;
- our ability to identify and develop new product candidates;
- our ability to protect and defend our intellectual property position and our reliance on third party licensors;
- our commercialization, marketing and manufacturing capabilities and strategy;
- market acceptance of our product candidates, the size and growth of those markets for our product candidates and any future product candidate we may seek to develop;
- the potential for changes to current regulatory mandates requiring health insurance plans to cover treatments or adequately reimburse patients for treatments utilizing our product candidates;
- our relationships with and the performance of our collaboration partners and their product candidates;
- our ability to develop sales and marketing capabilities;
- our ability to identify, recruit and retain key personnel;
- our expectations regarding the time during which we will be an emerging growth company under the Jumpstart Our Business Startups Act of 2012, or the JOBS Act;
- potential disruptions to our business; and
- projections relating to our competitors in the industry.

You should refer to the "Risk Factors" section of this Annual Report to Form 10-K and in our other filings with the Securities and Exchange Commission for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Annual Report on Form 10-K will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, these statements should not be regarded as representations or warranties by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

As used in this Annual Report on Form 10-K, unless otherwise stated or the context otherwise indicates, references to "Spring Bank," the "Company," "we," "our," "us" or similar terms refer to Spring Bank Pharmaceuticals, Inc. and our wholly owned subsidiaries.

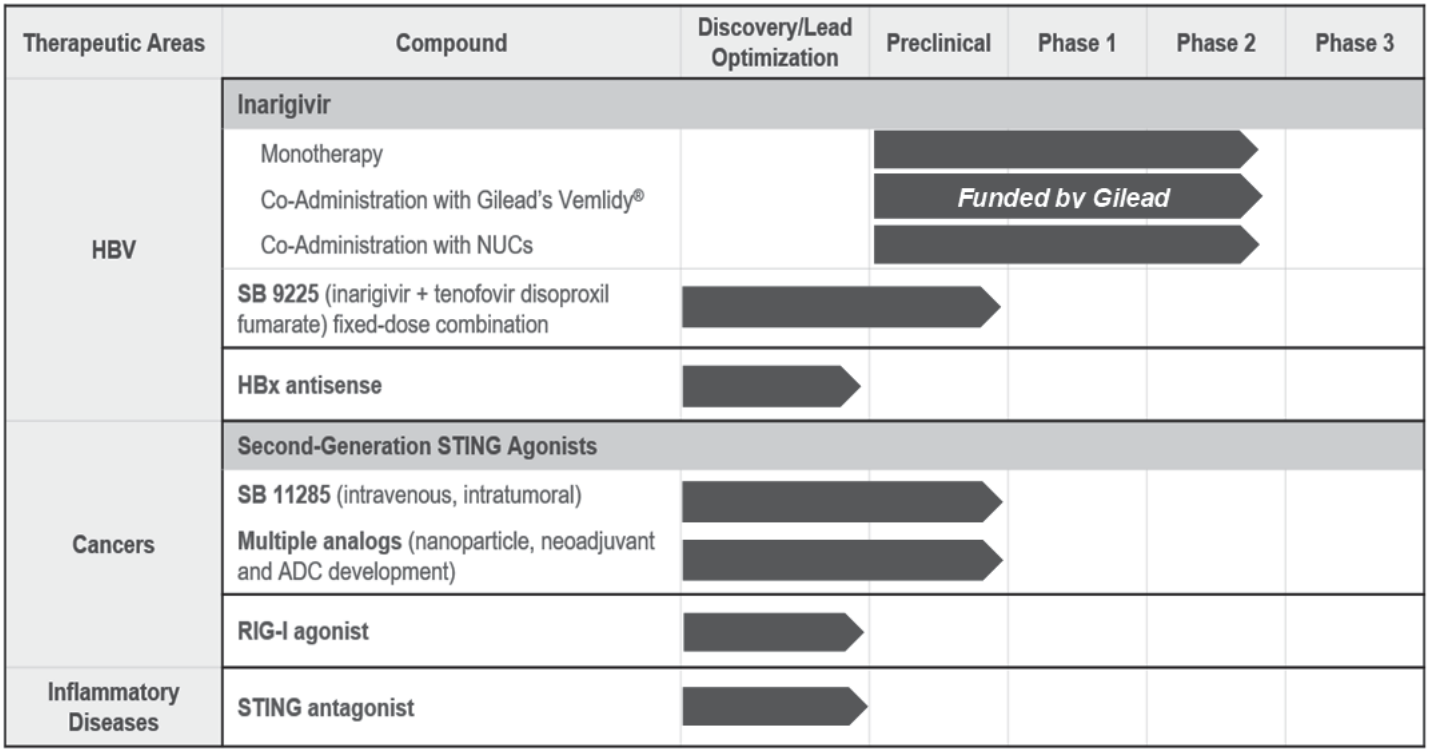
PART I

Item 1. Business

Overview

We are a clinical-stage biopharmaceutical company engaged in the discovery and development of a novel class of therapeutics for the treatment of viral infections, inflammatory diseases and certain cancers using our proprietary small molecule nucleotide platform. We design our compounds to selectively target and modulate the activity of specific proteins implicated in various disease states. We are developing our lead product candidate, inarigivir soproxil, or inarigivir, for the treatment of chronic hepatitis B virus, or HBV. We have designed our antiviral product candidates, including inarigivir, to selectively activate within infected hepatic cells the cellular protein, retinoic acid-inducible gene 1 (RIG-I), to inhibit viral replication and to cause the induction of intracellular interferon signaling pathways for antiviral defense. We believe that inarigivir, as a RIG-I agonist, could play an important role in antiviral therapy as a result of its dual mechanism of action that is designed to selectively modulate the body's immune response and inhibit viral replication. We are also developing additional product candidates, including our lead STING (STimulator of INterferon Genes) agonist product candidate, SB 11285, which is an immunotherapeutic agent for the potential treatment of selected cancers.

The following table summarizes the status of our development pipeline. We retain exclusive global commercial rights to all of our compounds.



Chronic HBV Program

Chronic HBV infection, which is defined by the presence of hepatitis B surface antigen, or HBsAg, for greater than six months, is a virus most commonly transmitted by contact with the blood or other bodily fluids of an infected person. Individuals with chronic HBV are at an increased risk of developing liver cancer, significant liver disease, or permanent scarring of the liver, leading to cirrhosis and liver failure. There is no approved cure for chronic HBV. Currently approved, standard of care therapies for the treatment of chronic HBV lack a broadly sustained response following the discontinuation of treatment and have significant limitations. Although treatment with pegylated interferon-α, or PEG-IFN- α, products can ultimately reduce the amount of HBV DNA, or viral load, in the body, this treatment only has a limited effect on the rate of loss or clearance of HBsAg. PEG-IFN- α products also have significant side effects, including flu-like symptoms and fever and, with long term use, can lead to suppression of the production of red and white blood cells, mood swings, depression, anxiety and other neuropsychiatric effects. Additionally, while nucleoside/tide analogue direct-acting oral antiviral agents such as entecavir (marketed by Bristol-Myers Squibb as Baraclude®), tenofovir disoproxil fumarate 300mg (TDF) (marketed by Gilead as Viread®), and tenofovir alafenamide 25mg (TAF) (marketed by Gilead as Vemlidy®), which we collectively refer to as "NUCs," have demonstrated that they potently suppress HBV DNA, which

generally we refer to as "viral suppression" or "virally-suppressed," they generally only suppress the virus during treatment without providing significant levels of HBsAg loss or clearance. Additionally, patients taking these NUCs likely require life-long treatment.

Experts and regulators have suggested that a "functional cure," characterized as either the loss of HBsAg or complete suppression of HBV DNA production, both of which are sustained off therapy, should be the goal of any new curative HBV therapy. A functional cure for chronic HBV with a shorter, finite period of treatment could improve clinical prognosis with a reduction in the risks of cirrhosis and liver cancer.

Inarigivir Clinical Trial Strategy. We are developing our lead product candidate, inarigivir, an orally-administered hepatic-selective immunomodulator, as a potential backbone in a combinatorial treatment for chronic HBV with the goal to accelerate and substantially increase chronic HBV functional cure rates in a simple, safe and selective manner.

ACHIEVE Trial. We are currently evaluating inarigivir for the treatment of chronic HBV in a global Phase 2 multi-center clinical trial of inarigivir, which we refer to as the ACHIEVE trial. The ACHIEVE trial is being conducted under our first clinical trial supply and collaboration with Gilead Sciences, Inc., or Gilead. Approximately 80 treatment-naive patients infected with chronic HBV have received doses of 25mg, 50mg, 100mg or 200mg of inarigivir or a placebo as a monotherapy administered daily for 12 weeks, followed by all patients receiving a sequential dose of Viread for 12 weeks. The active-placebo randomization schedule was 4:1 in the inarigivir monotherapy dosing period.

In the first three cohorts (25mg, 50mg and 100mg) of the ACHIEVE trial, 13 of 47 patients (28%) had a 0.5 $\log_{10}$ or greater reduction in HBsAg. Of these 13 responder patients, six were HBeAg-negative (-) patients and seven were HBeAg-positive (+) patients. Additionally, we have observed a dose dependent response of inarigivir on HBV DNA and HBV RNA over the first three cohorts. To date, inarigivir has been well tolerated in the ACHIEVE trial, with no inarigivir-related serious adverse events observed, and no flu-like symptoms or other interferon-like side effects.

All patients in the final 200mg cohort of the ACHIEVE trial have completed dosing of Viread and top-line results from the final 200mg cohort will be presented at The International Liver Congress, the Annual Meeting of the European Association for the Study of the Liver (EASL) in April 2019.

Gilead Collaboration. In July 2017, we entered into our second clinical trial collaboration agreement with Gilead under which Gilead is funding and conducting a Phase 2 clinical trial examining the co-administration of inarigivir and Vemlidy in patients infected with chronic HBV. This clinical trial collaboration was expanded in August 2018 to include two additional cohorts. In the first cohort of this Phase 2 trial, treatment-naive patients received 12 weeks of combination therapy with inarigivir 50mg and Vemlidy, while in the second cohort treatment-naive patients are receiving 12 weeks of combination therapy with inarigivir 200mg and Vemlidy. In a third cohort, Gilead is evaluating the administration of inarigivir 100mg in virally-suppressed patients who are already are and continue to be treated with a NUC. While we have approved the protocol for this trial under a joint steering committee, Gilead is conducting this trial at their own expense.

CATALYST Trials. We plan to initiate in the first half of 2019 two major Phase 2 global trials examining the administration of inarigivir 400mg in different patient populations and under different dosing regimens. We anticipate that the first global trial will be conducted in Asia and the U.S. and will evaluate non-cirrhotic, treatment-naïve HBeAg positive and negative patients infected with chronic HBV who receive inarigivir 400mg as both(i) monotherapy for 12 weeks followed by the sequential treatment of Vemlidy for 12 weeks, and (ii) in combination with Vemlidy for 24 weeks. We refer to this trial as the CATALYST 1 trial. Pre-defined responder patients at week 24 will continue to receive inarigivir 400mg and Vemlidy for up to an additional 24 weeks to determine if they are able to achieve a functional cure.

Concurrent with the CATALYST 1 trial, we plan to initiate a separate trial, which we refer to as the CATALYST 2 trial, in the United Kingdom and Canada examining the use of inarigivir 400mg in non-cirrhotic, virally-suppressed patients currently on a NUC (i) following the cessation of treatment with a NUC, which we refer to as "Stop and Shock" treatment, and (ii) with the continued dosing of a NUC, which we refer to as "Suppress and Shock" treatment. Under the "Stop and Shock" treatment, patients will receive inarigivir 400mg for 24 weeks and then stop all treatment to evaluate for loss of HBsAg or sustained viral suppression over time, up to 18 months. Under the "Suppress and Shock" treatment, patients will receive inarigivir 400mg, in addition to their current NUC treatment, for a period of 24-48 weeks, and again stop all treatment with a follow up to see if there is either loss of HBsAg or sustained viral suppression off treatment. Pending preliminary results from the CATALYST studies, we plan to conduct a separate "Suppress and Shock" trial in the United States and the European Union, potentially in the second half of 2019. This trial could evaluate the efficacy of inarigivir 400mg over the course of 48 weeks in virally-suppressed patients when compared to the use of a NUC alone.

The CATALYST trial designs allow for evaluation of the likelihood of functional cure and have the potential ability to define the design of Phase 3 trials to allow for a regulatory strategy for the co-administration of inarigivir with a NUC and inarigivir

monotherapy in selected chronic HBV patient populations. The ability to continue treatment for up to 48 weeks and the stopping of treatment with follow up to look for sustained response will define whether inarigivir, when combined with a NUC alone or as a finite monotherapy in "Stop and Shock," is adequate in either treatment-naïve or virally-suppressed patient populations.

We anticipate reporting interim top-line results from the CATALYST trials throughout 2020 and into 2021.

Fixed-Dose Combination (SB 9225). We are also pursuing the development of SB 9225, a co-formulation of inarigivir with tenofovir disoproxil fumarate, as a potential fixed-dose combination product for the treatment of patients with chronic HBV. We have conducted early development work that indicates compatibility of inarigivir with Viread in the same formulation. We have conducted additional formulation development work for SB 9225 and successfully manufactured initial quantities of SB 9225. The introduction of SB 9225, if approved, could potentially result in enhanced patient compliance and allow for a more favorable safety profile. Subject to the results of our Phase 2 inarigivir trials, we could be in a position to initiate a Phase 3 program for SB 9225 in the United States, Europe and Asia in 2020.

Inarigivir Strategic Collaborations. The treatment of chronic HBV is complex and heterogenous, and we believe that any curative treatment will require a combinatorial approach. Although our initial approach has been to evaluate inarigivir in combination with NUCs (*see "Gilead Collaboration" above*), we have explored pre-clinical studies of inarigivir with novel drugs with different pharmacological mechanisms of action than a NUC. Accordingly, we intend to enter into additional collaborations to develop inarigivir with products or product candidates that have different pharmacological mechanisms of action than inarigivir or a NUC. Specifically, we are considering novel combination opportunities for inarigivir, including combination with siRNA compounds, core protein allosteric modifiers (CpAMs) and toll-like receptor 8 (TLR8) or programmed cell death protein 1 (PD-1) inhibitors. We anticipate that inarigivir, together with a NUC, will be included in at least one "triple combination" clinical trial with a siRNA compound or a different mechanism in 2019.

Immuno-Oncology Program

We have identified multiple STING agonist compounds as potential immunotherapeutic agents for the treatment of selected cancers. Recent published scientific literature indicates that the activation of the STING pathway can result in the induction of cellular interferons and cytokines and promote a strong anti-tumor response through the induction of innate and adaptive immune responses. We believe that the distinctive chemistry that we use to develop our STING agonists allows for conjugation with other therapeutic modalities, including but not limited to nanoparticle formulation and antibody drug conjugates, or ADCs, for targeted delivery and potential for improved tolerability, safety and efficacy.

We are developing our lead STING agonist product candidate, SB 11285, as a second-generation immunotherapeutic agent for the treatment of selected cancers. In our preclinical studies in multiple tumor-derived cell lines, SB 11285 has been observed to cause the induction of cytokines consistent with engagement of the STING target, as well as cell death and apoptosis. Based on our preclinical studies performed to date, SB 11285 has reduced tumor volumes in multiple rodent tumor models when administered intravenously or intratumorally. These findings lead us to believe that SB 11285 has the potential to be administered clinically by either route of administration, and that SB 11285 may be used to target a variety of tumors at various anatomic sites and, if approved, has the potential to be used in combination with other therapeutic modalities to enhance efficacy.

We are currently advancing the SB 11285 program with preclinical, toxicology, and process development efforts. Subject to the results of these preclinical studies, we anticipate that we will submit an investigational new drug application, or IND, for SB 11285 in the second quarter of 2019, and, if approved, initiate a Phase 1/2 clinical trial in cancer later in 2019. SB 11285 could be the first intravenously-administered STING agonist product candidate to enter clinical development.

Intellectual Property Estate

As of December 31, 2018, we had a global intellectual property portfolio consisting of 70 issued patents worldwide and hold multiple patent applications directed to our lead product candidate, together with trade secrets and know-how. As of December 31, 2018, we held one U.S. patent, one European patent and multiple other foreign patents with claims covering the composition of matter of inarigivir that begin to expire in December 2026 and a second U.S. patent with claims covering the composition of matter of inarigivir that expires in June 2030, in each case, without considering any potential patent term adjustments or extensions. We hold U.S. and international patent applications with claims covering the composition of matter of SB 11285. If any of these SB 11285 patent applications are issued, the patents would begin to expire in 2037, without considering any potential patent term adjustments or extensions.

Our Technology

Nucleotides and nucleic acids bind to the active sites of proteins as part of normal cellular processes in order to regulate biological functions. Proteins can bind either directly to nucleic acids or indirectly through an alternative nucleic acid-protein complex. Modulating these interactions through agonism (producing or encouraging binding) and antagonism (limiting or discouraging binding) affords potentially broad therapeutic potential and provides an opportunity to target proteins and their biological functions that are typically considered challenging with current modalities.

We design our compounds to modulate the interaction between nucleotides or nucleic acids and proteins. Because our compounds resemble naturally occurring nucleotides and nucleic acids in the body, we believe they can be more efficient in modulating the interactions with proteins through higher selectivity than traditional small molecule approaches.

We have focused our research on the optimization of our novel compounds with favorable drug attributes using various approaches including rational drug design, combinatorial chemistry, structural biology and phenotypic screening approaches. By making specific structural modifications to our compounds, we enable them to bind to targets in the diseased tissues with high affinity and selectivity.

Unlike other nucleic acid-based approaches that act by inhibiting specific protein expression through downregulation of messenger RNA, such as RNA interference, compounds act directly on proteins and therefore can be used to either upregulate or downregulate the activities of the proteins that play a role in disease processes. We have designed inarigivir to bind selectively to and activate RIG-I, a protein that is involved in the activation of the body's immune response to foreign pathogens.

Some distinguishing features of compounds within our platform include:

- ***Novel mechanisms of action.*** Inarigivir and our other novel compounds are designed to inhibit viral replication through two mechanisms:(i) a direct acting anti-viral (DAA) mechanism where inarigivir acts a non-nucleotide reverse transcriptase inhibitor (NNRTI) to inhibit the interaction of pre-genomic RNA, or pgRNA, and HBV DNA polymerase within the replication complex; and (ii) binding to RIG-I with activation within the hepatocyte of the innate immune response through production of natural immunomodulatory cytokines, including type I and II interferons. Viruses have evolved mechanisms to block the protective effects of interferon production. Our compounds are designed to restore interferon production in infected cells. In the case of chronic HBV, we believe that induction of the innate immune response is required for loss or clearance of HBsAg and the achievement of a functional cure.

- ***Multiple routes of delivery, including oral administration.*** Because our novel compounds have small molecule characteristics, they can be delivered orally. Additionally, our compounds potentially may be delivered intravenously and through intra-nasal and inhalation delivery, depending on the target disease. We believe that the versatility of our compounds may allow us to design compounds that use the optimal delivery approach for the target disease.

- ***Potential to treat a broad range of viral, inflammatory and oncological diseases.*** We design our compounds to selectively target certain proteins whose presence or activity contributes to disease severity or causes the underlying disease. We believe that this approach is potentially applicable to a broad range of viral, inflammatory and oncological diseases.

- ***Selective immune response.*** Certain of our compounds are designed to trigger a specific immune response in virally infected cells. To date, we have not observed a nonspecific, extra-hepatic immune response in our completed preclinical and clinical trials of inarigivir. Our STING agonists are designed to activate immune cells for efficient immune-mediated anti-tumor response.

- ***Potential for use in combination with other antiviral agents.*** Because our compounds are designed to act by an immunomodulatory function, we believe they may be developed for use in combination with other antiviral agents that act against viral disease by different mechanisms of action.

Our HBV Program

We have two compounds in development for the treatment of chronic HBV, including our lead product candidate inarigivir. We have designed our HBV product candidates to selectively activate within infected hepatic cells the cellular protein, RIG-I, to inhibit viral replication and to cause the induction of intracellular interferon signaling pathways for antiviral defense.

Interferon is an immunomodulatory cytokine with potent antiviral activity. Interferon activates both innate and adaptive immune responses in infected cells. The innate immune response is the first line of defense against virus infection before the adaptive immune response is induced. It is well established that the innate immune response is critical to restricting virus replication and infection. The adaptive immune system is part of the overall immune system and is required to eliminate or prevent pathogen growth. Adaptive immunity creates immunological memory after an initial response to a specific pathogen and leads to an enhanced response to subsequent encounters with that pathogen.

RIG-I is inactive in uninfected cells but is activated when a cell is virally infected. The activation of RIG-I results in the production of interferon within the cells through a well-regulated signaling pathway. Viruses invade cells and are able to replicate and spread because they have mechanisms to block the protective effects of antiviral signaling proteins, such as RIG-I. Viral genomes encode proteins that can block interferon synthesis and signaling, inhibit the function of interferon-induced antiviral proteins and produce interferon receptor decoy molecules to prevent induction of interferon signaling. Thus, by turning off interferon production and function, viruses abrogate the immune response, which enables them to multiply rapidly in cells.

Inarigivir is designed to inhibit viral replication through two mechanisms:(i) a direct acting anti-viral (DAA) mechanism where inarigivir acts a non-nucleotide reverse transcriptase inhibitor (NNRTI) to inhibit the interaction of pgRNA and HBV DNA polymerase within the replication complex; and (ii) binding to RIG-I with activation within the hepatocyte of the innate immune response through production of natural immunomodulatory cytokines, including type 1 and II interferons. Given these novel host-targeted mechanisms of action of inarigivir and its potential ability to cause the loss or clearance of HBsAg, we plan to develop inarigivir primarily in combination with currently marketed and investigational direct-acting oral antiviral agents or other treatments with differing mechanisms of action.

We have not yet submitted an IND application to the United States Food and Drug Administration, or FDA, and may not conduct any clinical trial for inarigivir in the United States until we submit an IND to the FDA. We intend to submit an IND to the FDA for inarigivir in 2019.

Current Standard of Care for Chronic HBV Lacks a Sustained Response

There is no approved cure for chronic HBV. The current standard of care treatments for chronic HBV include PEG-IFN-α products and direct-acting oral antiviral agents, which we refer to as NUCs.

A PEG-IFN-α product is an antiviral medication administered by injection in which the chemical substance known as polyethylene glycol, or PEG, is chemically attached to interferon-α to improve the duration of effect of interferon-α. Interferon-α is a protein that interferes with viral replication within host cells. In Europe, PEG-IFN-α products are indicated for first line treatment of chronic HBV virus according to guidelines of the European Association for the Study of the Liver for chronic HBV treatment for certain patient populations. However, PEG-IFN-α products have significant limitations. Although treatment with PEG-IFN-α products can reduce the amount of HBV DNA in the body, the treatment only has a minor effect on the rate of HBsAg reduction or loss. PEG-IFN-α products also have significant side effects, including flu-like symptoms and fever and, with long term use, can lead to suppression of the production of red and white blood cells, mood swings, depression, anxiety and other neuropsychiatric effects.

Direct-acting oral antiviral agents for chronic HBV, such as Baraclude, Viread and Vemlidy, have demonstrated they suppress viral replication. These direct-acting oral antiviral agents are potent suppressors of HBV DNA, but generally only suppress the virus during treatment without providing significant loss or clearance of HBsAg, and patients taking these antiviral agents require potentially life-long treatment.

Experts and regulators have suggested that a "functional cure," characterized by sustained loss of HBsAg with or without hepatitis B surface antibody conversion, should be the goal of any new curative HBV therapy. Studies have indicated that the current functional cure rate, when combining PEG-IFN-α and Viread over a 48-week treatment period, is less than 10%. According to an article published in the Journal of Hepatology in August 2017, experts believe that for any future treatment to significantly increase the current functional cure rate, an immunomodulatory agent will likely be a necessary component of therapy.

There is a significant unmet need for a chronic HBV treatment that can be administered orally with a favorable safety profile. We believe that the immunomodulatory activity of inarigivir could become a key component of a future combinatorial treatment for patients infected with chronic HBV, potentially increasing the percentage of chronic HBV patients who achieve a functional cure. Specifically, a functional cure with a shorter, finite period of treatment could improve clinical prognosis with a reduction in the risks of cirrhosis and liver cancer.

Early Decline in HBsAg at Week 12 Represents a Key Predictor of Response and Eventual Loss of HBsAg for Interferon and Perhaps Other Immunomodulators in HBV. Reduction in HBsAg following 12 weeks of treatment, either with monotherapy PEG-IFN-α or the combination of PEG-IFN-α with a direct-acting oral antiviral agent, has been reported by researchers as a predictive biomarker of response and eventual loss of HBsAg in patients with chronic HBV.

In a report published in Hepatology in 2013, researchers presented the results of a pooled analysis of over 800 participants from three global HBV trials in which HBsAg decline following 12 weeks of treatment with either monotherapy PEG-IFN-α or the combination of PEG-IFN-α with the oral antiviral Epivir-HBV (lamivudine) was predictive of six-month post-treatment response rates in patients with chronic HBV (26% response rate with HBsAg decline at 12 weeks compared to 14% response rate with no HBsAg decline at 12 weeks). In this analysis, treatment response was defined as a composite endpoint of HBeAg loss with an HBV DNA level <2,000 IU/mL or HBsAg loss at 24 weeks after the end of treatment.

Separately, in November 2014, at the annual meeting of the American Association for the Study of Liver Diseases (AASLD)—The Liver Meeting, Gilead presented data from a randomized trial evaluating various treatment cohorts, including monotherapy with PEG-IFN-α, monotherapy with Viread, and the combination of PEG-IFN-α and Viread, in 740 patients with chronic HBV. Overall, HBsAg loss was only observed in patients receiving PEG-IFN-α either alone or in combination with Viread. The combination arm of PEG-IFN-α and Viread demonstrated that only 7.3% of patients had HBsAg loss at Week 48 of treatment, which was predicted by a greater than 0.5$\log_{10}$ reduction in HBsAg at Week 12 of treatment. A 1.0 $\log_{10}$ reduction means a 90% lower virus level in the treated patient from baseline.

Based on the reported findings and inarigivir's observed ability to induce intracellular interferon signaling pathways, we believe that our assessments of HBsAg decline at Week 12 in our ACHIEVE clinical trial and the clinical trial that Gilead is conducting may be indicative of inarigivir's ability to cause the loss or clearance of HBsAg in treated patients following a longer duration of treatment.

Novel biomarkers that measure the initial production of pgRNA from covalently closed circular DNA, or cccDNA, such as serum HBV RNA, are emerging as important early serum predictors of inhibition of viral replication and may help guide combination strategies for clinical trial development and regulatory pathways. Multiple companies developing drug candidates, including siRNAs targeting HBV and HBV-specific capsid inhibitors, are exploring the utility of this novel biomarker. HBV RNA is a secondary endpoint in our ACHIEVE trial to enable us to evaluate its utility as a predictor for HBsAg loss.

Clinical Development of Inarigivir

Inarigivir is being evaluated for the treatment of chronic HBV in multiple worldwide clinical trials. Based on the preclinical and clinical data we have generated to date, as well as the safety demonstrated in our Phase 1 clinical trial of inarigivir in patients with hepatitis C virus, or HCV, we believe inarigivir may induce an antiviral immune response during chronic HBV infection and cause loss or clearance of HBsAg without the side effects associated with PEG-IFN-α products. We believe that by reducing HBsAg, inarigivir has the potential to provide a functional cure for chronic HBV patients when used in combination with other antiviral agents, thus leading to a finite and shorter duration of treatment.

ACHIEVE Trial. In 2016, we initiated the ACHIEVE trial in patients with chronic HBV to explore the use of inarigivir as a monotherapy for 12 weeks, followed by treatment with Viread for 12 weeks, in a clinical trial collaboration with Gilead. We conducted the ACHIEVE multi-center clinical trial of inarigivir in Canada, Hong Kong, Korea and Taiwan to enable us to select appropriate dose level(s) to move forward into additional clinical trials and to provide us with the necessary safety and efficacy data to study the combined use of inarigivir and Viread. The ACHIEVE trial is a randomized, placebo-controlled, multiple ascending dose trial in up to 100 non-cirrhotic patients infected with chronic HBV using doses of 25mg, 50mg, 100mg and 200mg of inarigivir as a monotherapy administered daily for 12 weeks. Following this treatment, all patients will receive treatment with Viread as a monotherapy for 12 weeks. Patients will be sequentially enrolled into one of the four dose cohorts and randomized between an inarigivir dose group or placebo on a 4:1 basis. Patients will be stratified based on HBeAg (+/-) status. HBeAg is a non-structural protein which is secreted by the virus and whose presence in blood, or HBeAg(+), is indicative of wild type or non-mutated virus with high levels of viral replication. The loss of HBeAg occurs secondary to mutations in the virus and results in a patient becoming HBeAg(-) with a resulting lower level of actively replicating virus. The primary endpoints of the ACHIEVE trial are safety and antiviral activity, as measured by the change in HBV DNA at week 12 from baseline. Multiple exploratory secondary endpoints include reduction or loss of HBsAg, HBeAg and HBV RNA.

In the first three cohorts (25mg, 50mg and 100mg) of the ACHIEVE trial, 13 of 47 patients (28%) had a 0.5 $\log_{10}$ or greater reduction in HBsAg. Of these 13 responder patients, six were HBeAg-negative (-) patients and seven were HBeAg-positive (+) patients. Additionally, we observed a dose dependent response of inarigivir on HBV DNA and HBV RNA, and of the 16 HBeAg-negative patients who had detectable HBV RNA at baseline, nine had undetectable HBV RNA at the end of the 12-week monotherapy dosing regimen. Blood levels of HBsAg and HBV RNA are generally viewed as biomarkers for the presence of active cccDNA,

which is the major reservoir for chronic HBV and the template for viral replication. Accordingly, reductions in HBsAg and HBV RNA have been associated with clearance of ccc DNA. Inarigivir responses have been proportional to the baseline HBsAg level and we believe are reflective of the mechanism of action of inarigivir as an immunomodulator. Baseline HBsAg level < 10,000 IU ($4\log_{10}$) remains the strongest predictor of response to inarigivir across all cohorts for HBV DNA and HBV RNA reductions irrespective of HBeAg status. This response is consistent with the known role of HBsAg as a down regulator of the host immune response to HBV. To date, inarigivir has been well tolerated in the ACHIEVE trial, with no inarigivir-related serious adverse events observed. Treatment-emergent adverse events have ranged from mild to moderate in severity, with no flu-like symptoms or other interferon-like side effects. One clinical serious adverse event of knee pain likely unrelated to inarigivir and one biochemical event of a transient, non-sustained Grade 3 hypertryglyceridemia were observed.

All patients in the final 200mg cohort of the ACHIEVE trial have completed dosing of Viread and top-line results from the final 200mg cohort will be presented at The International Liver Congress, the Annual Meeting of the European Association for the Study of the Liver (EASL) in April 2019.

Gilead Clinical Trial Supply and Collaboration Agreement. In July 2017, we entered into our second collaboration agreement with Gilead, which was amended in August 2018 to expand the collaboration. Under this clinical trial supply and collaboration agreement, Gilead is funding and conducting a Phase 2 clinical trial examining (i) the co-administration of inarigivir and Vemlidy and (ii) the evaluation of inarigivir in chronic HBV patients whose viral load is suppressed. In the first cohort, 30 treatment-naive patients infected with chronic HBV received 12 weeks of combination therapy with inarigivir 50mg and Vemlidy. In the second cohort, up to 30 treatment-naive patients infected with chronic HBV are receiving 12 weeks of combination therapy with inarigivir 200mg and Vemlidy. All patients in the first two cohorts will also receive Vemlidy as a monotherapy for 36 weeks. In a third cohort, Gilead is evaluating the administration of inarigivir 100mg in chronic HBV patients whose viral load is suppressed and who are already being treated with a NUC.

CATALYST 1 and CATALYST 2 Trials. We plan to initiate in the first half of 2019 two major Phase 2 global trials examining the administration of inarigivir 400mg in different patient populations and under different dosing regimens.

We anticipate that the first global trial, the CATALYST 1 trial, will be conducted in Asia and the U.S. and will evaluate in up to 60 treatment-naïve HBeAg positive and negative patients. Under this response-guided trial, patients will be randomly assigned to one of the following three arms: (i) 20 patients will receive inarigivir 400mg monotherapy daily for 12 weeks followed by the sequential treatment of Vemlidy for 12 weeks; (ii) 20 patients will receive inarigivir 400mg monotherapy three times per week for 12 weeks followed by the sequential treatment of Vemlidy for 12 weeks; and (iii) 30 patients will receive inarigivir 400mg in combination with Vemlidy for 24 weeks. Pre-defined responder patients at week 24 will continue to receive inarigivir 400mg and Vemlidy for up to an additional 24 weeks to determine if they are able to achieve a functional cure.

Concurrent with the CATALYST 1 trial, we plan to initiate the CATALYST 2 trial in the United Kingdom and Canada examining the use of inarigivir 400mg. We anticipate that this trial will evaluate up to 60 virally-suppressed patients currently on a NUC (i) following the cessation of treatment with a NUC, which we refer to as "Stop and Shock" treatment, and (ii) with the continued dosing of a NUC, which we refer to as "Suppress and Shock" treatment. Under the "Stop and Shock" treatment, 20 patients will receive inarigivir 400mg for 24 weeks and then stop all treatment to evaluate for loss of HBsAg or sustained viral suppression over time, up to 18 months. Under the response-guided "Suppress and Shock" treatment, 40 patients will receive inarigivir 400mg, in addition to their current NUC treatment, for a period of 24-48 weeks, and again stop all treatment with a follow up to see if there is either loss of HBsAg or sustained viral suppression off treatment. The CATALYST 2 trial will include specialized fine needle aspirations of the liver to evaluate intra-hepatic immune responses.

Pending preliminary results from the CATALYST studies, we plan to conduct a separate "Suppress and Shock" trial in the United States and the European Union, potentially in the second half of 2019. This trial could evaluate the efficacy of inarigivir 400mg over the course of 48 weeks in virally-suppressed patients when compared to the use of a NUC alone.

The CATALYST trial designs allow for evaluation of the likelihood of functional cure and have the potential ability to define the design of Phase 3 trials to allow for a regulatory strategy for the co-administration of inarigivir with a NUC and inarigivir monotherapy in selected chronic HBV patient populations. The ability to continue treatment for up to 48 weeks and the stopping of treatment with follow up to look for sustained response will define whether inarigivir, when combined with a NUC alone or as a finite monotherapy in "Stop and Shock," is adequate in either treatment-naïve or virally-suppressed patient populations.

We anticipate reporting interim top-line results from the CATALYST trials throughout 2020 and into 2021.

Liver Biopsy Study. We plan to conduct a single center study in Singapore to evaluate the intra-hepatic activation of the immune response by inarigivir and to correlate immunology findings with the effect on HBV intra-hepatic virology, in particular cccDNA. In this study, eight virally-suppressed patients with chronic HBV will receive inarigivir 400mg daily to three times a week

and have liver biopsies before treatment and at week six on treatment. Liver biopsies will undergo specialized immunology and virology studies to correlate and confirm the intra-hepatic mechanism of action on both immune function and HBV replication. We anticipate reporting initial results from this study in late 2019.

Other Development Efforts for Chronic HBV

SB 9225 Fixed-Dose Combination. We are also pursuing the development of SB 9225, a co-formulation of inarigivir with tenofovir disoproxil fumarate, as a potential fixed-dose combination product for the treatment of patients with chronic HBV. We have conducted early development work that indicates compatibility of inarigivir with Viread in the same formulation. We have conducted additional formulation development work for SB 9225 and successfully manufactured initial quantities of SB 9225. The introduction of SB 9225, if approved, could potentially result in enhanced patient compliance and allow for a more favorable safety profile. Subject to the results of our Phase 2 inarigivir trials, we could be in a position to initiate a Phase 3 program for SB 9225 in the United States, Europe and Asia in 2020.

HBx Antisense Program. Recent scientific literature has established the important role of the HBx gene in the life cycle of the Hepatitis B virus and in the development of hepatocellular carcinoma (HCC) and identified HBx as a promising target for the treatment of HBV. We are developing novel antisense oligonucleotide compounds to block HBx expression in HBV patients. We are evaluating these compounds to assess their potential as product candidates.

Other Strategic Initiatives for Chronic HBV

The treatment of chronic HBV is complex and heterogenous, and we believe that any curative treatment will require a combinatorial approach. Although our initial approach has been to evaluate inarigivir in combination with NUCs (*see "Gilead Clinical Trial and Supply Collaboration Agreement" above*), we have explored pre-clinical studies of inarigivir with novel drugs with different pharmacological mechanisms of action than a NUC. Accordingly, we intend to enter into additional clinical collaborations with others to develop inarigivir with products or product candidates that have different pharmacological mechanisms of action than inarigivir or NUCs. Specifically, we are considering novel combination opportunities for inarigivir, including combination with siRNA compounds and CpAMs and TLR8 or PD-1 inhibitors. We anticipate that inarigivir, together with a NUC, will be included in at least one "triple combination" clinical trial with a siRNA compound or a different mechanism in 2019.

Immuno-Oncology Program

In addition to our HBV clinical program, we are also developing multiple compounds for the potential treatment of selected cancers.

STING Agonist Program

We have developed multiple STING agonist compounds, which are differentiated cyclic dinucleotides, as potential immunotherapeutic agents for the treatment of selected cancers. Immunotherapy has emerged in recent years as a transformative approach for the treatment of cancer because the induction of interferons and interferon-stimulated genes in tumor cells and within the tumor microenvironment is essential for modulating the host-immune response and inducing apoptosis of tumor cells. Recent published scientific literature indicates that the activation of the STING pathway can result in the induction of cellular interferons and cytokines and promote a strong anti-tumor response through the induction of innate and adaptive immune responses.

SB 11285. We are developing our lead STING agonist product candidate, SB 11285, as a second-generation immunotherapeutic agent for the treatment of selected cancers. In our preclinical studies in multiple tumor-derived cell lines, SB 11285 has been observed to cause the induction of cytokines consistent with engagement of the STING target, as well as cell death and apoptosis. Based on our preclinical studies performed to date, SB 11285 has demonstrated efficacy in multiple syngeneic rodent tumor models when administered intravenously or intratumorally. These findings lead us to believe that SB 11285 has the potential to be administered clinically by either route of administration and enables SB 11285 to target a variety of tumors at various anatomic sites.

We are currently advancing the SB 11285 program with preclinical, toxicology, and process development efforts. We anticipate that we will submit an IND for SB 11285 in the second quarter of 2019, and, if approved, initiate a Phase 1/2 clinical trial in cancer later in 2019. SB 11285 could be the first intravenously-administered STING agonist product candidate to enter clinical development.

Combination of STING Agonists with New Therapeutic Modalities. We believe the chemistry used to develop our STING agonists also allows for site-specific conjugation to other therapeutic modalities including antibodies to form antibody drug conjugates, or ADCs. The formulation of our STING agonists in combination with an antibody to form an ADC could provide

targeted delivery to the tumor via a bio-reversible linker that is designed to release the STING agonist at the tumor site. We are also developing a nanoparticle formulation for systemic delivery of our STING agonists. In *in vitro* studies involving the use of a nanoparticle formulation of SB 11285, we have observed potent STING agonist activity. Both of these approaches may distinguish the profile and widen the therapeutic index of SB 11285 by enabling its delivery to the target cells to effect tumor clearance.

RIG-I Agonist Program

Spring Bank is building upon its expertise and experience in discovering and developing inarigivir, a RIG-I agonist, to discover and develop new novel RIG-I agonists specifically for potential oncology indications.

Other Early Research &Development Programs

STING Antagonist Program

In addition to our pipeline of antiviral and immune-oncology product candidates, we plan to explore the use of novel STING antagonist compounds for the treatment of certain autoimmune and inflammatory diseases. Our STING antagonists are designed to block aberrant STING-dependent signaling that contribute to inflammatory diseases. We are optimizing different structural classes to develop lead compounds for autoimmune and inflammatory diseases.

Patents and Proprietary Rights

Our success will depend upon our ability, and upon the ability of any future collaborators of ours, to obtain and maintain intellectual property protection in the United States and other key pharmaceutical markets around the world for our product candidates and technologies, defend and enforce our intellectual property rights, preserve the confidentiality of our trade secrets and operate without infringing valid and enforceable intellectual property rights of others. We have sought, and plan to continue to seek, patent protection in the United States and other key pharmaceutical markets, that is intended to cover the composition of matter of our product candidates, their methods of use, related technologies and other inventions that are important to our business. In addition to patent protection, 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.

We have devoted considerable effort and resources to build a substantial patent estate designed to provide multiple levels of protection for our product candidates. As of December 31, 2018, we licensed two and owned more than 20 patent families. These patent families include nearly 200 patents and patent applications worldwide, including 12 patents and 38 patent applications in the United States and 58 patents and 90 patent applications outside the United States. Of these patents, four U.S. patents and five patents outside of the United States are subject to our license with BioHEP Technologies Ltd., or BioHEP. The licensed families include the active ingredient in inarigivir, i.e., SB 9000, and methods of assembling libraries of our compounds. Our patents and patent applications include protection for:

- compositions of matter for our compounds;
- processes for synthesizing and manufacturing our compounds;
- methods of using our compounds to treat or prevent disorders such as microbial infections, including dosage forms and formulations and methods relating to course of treatment; and
- methods of assembling libraries of our compounds.

With respect to inarigivir, as of December 31, 2018, we held one U.S. patent with claims covering the composition of matter of inarigivir specifically, pharmaceutical compositions, methods of treating HBV and methods of preparing inarigivir. This patent is expected to expire in December 2026, without considering any potential patent term extensions. As of December 31, 2018, we also held one U.S. patent covering the composition of matter of inarigivir generically, methods of treating HBV, including combination therapy with other agents and treatment of resistant strains of HBV. With patent term adjustment, this patent is expected to expire in June 2030, without considering any potential patent term extensions. This patent has been granted in the European Patent Office and has been nationalized in all the major countries in Europe. These nationalized patents, when issued, are expected to begin to expire in December 2026. We hold patents that have been granted in China, Japan and Korea with claims covering the active ingredient in inarigivir, and methods of using this compound. These patents are expected to begin to expire in 2022. We also hold patent applications that cover methods of using inarigivir, including in viral infections such as HBV and HCV. These patent applications, if issued, will begin to expire in 2031. In addition, we hold patent applications with claims covering the composition of matter of inarigivir generically and specifically in China, Europe, Hong Kong and India, which, if issued, are expected to begin to expire in December 2026.

We hold U.S. and foreign patent applications, which include methods of using inarigivir in various diseases, including certain resistant strains of infections such as HBV and HCV. If these patent applications are issued, the patents would be expected to begin to expire in 2037, without considering any potential patent term extensions.

We hold U.S. provisional patent applications, international (PCT) patent applications, and foreign patent applications which include claims to compositions of matter and various methods of using our STING agonists, including SB 11285, in oncology. If any of these patent applications are issued, the patents would be expected to begin to expire in 2037, without considering any potential patent term adjustments or extensions.

In each case, we own or hold the exclusive license to the foregoing patents and patent applications. We are not aware of any contested proceeding or third-party claims that cover any of our patents or patent applications.

The actual protection afforded by a particular patent varies from country to country and depends upon many factors, including the type of patent, the scope of its coverage and the availability of legal remedies in the country in which it issued.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application.

In the United States, the term of a patent covering an FDA-approved drug may be eligible for a patent term extension under the Hatch-Waxman Act as compensation for the loss of patent term during the FDA regulatory review process. The period of extension may be up to five years beyond the expiration of the patent but cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent among those eligible for an extension may be extended. Similar provisions are available in Europe and in certain other jurisdictions to extend the term of a patent that covers an approved drug. It is possible that issued U.S. patents covering inarigivir may be entitled to patent term extensions. If our product candidates receive FDA approval, we intend to apply for patent term extensions, if available, to extend the term of patents that cover the approved product candidates. We also intend to seek patent term extensions in any jurisdictions where they are available, however, there is no guarantee that the applicable authorities, including the FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

BioHEP License

In January 2016, we entered into an amended and restated license agreement, or the amended license agreement, with BioHEP which amended and restated our prior license agreement with BioHEP which we entered into in December 2003. The amended license agreement became effective on February 1, 2016. Under the amended license agreement, BioHEP granted us an exclusive worldwide license under certain patents and know-how to make, have made, use, sell, offer to sell and import certain product candidates comprising a novel phosphorothioate dinucleotide and certain related compounds, which include inarigivir, SB 9400, SB 9941 and SB 9946, for the diagnosis and/or treatment of all viral diseases and conditions.

We are solely responsible, at our expense, for conducting all research, development and commercialization activities with respect to licensed products.

Under the terms of the original license agreement, we issued to BioHEP 12,500 shares of our common stock and 1,000,000 shares of our series A preferred stock, which shares of Series A preferred stock were converted into 250,000 shares of our common stock in connection with our initial public offering in May 2016. In connection with entering into the amended license agreement, we issued to BioHEP an additional 125,000 shares of our common stock and issued to BioHEP a warrant to purchase an additional 125,000 shares of our common stock at a purchase price of $16.00 per share, which warrant expired unexercised on August 1, 2018. Under the license agreement, BioHEP is eligible to receive up to $3.5 million in development and regulatory milestone payments for disease(s) caused by each distinct virus for which we develop licensed product(s). BioHEP is also eligible to receive tiered royalties in the low-to-mid single-digits on net product sales of licensed products by us and our affiliates and sublicensees, and a specified share of non-royalty sublicensing revenues we and our affiliates receive from sublicensees, which share of sublicensing revenues is capped at a maximum aggregate of $2.0 million under all such sublicenses.

BioHEP's royalty rights generally extend on a licensed product-by-licensed product and country-by-country basis until the expiration of the last-to-expire of the BioHEP patent rights licensed to us or of patent rights claiming specified improvements that we own that cover the licensed product in the applicable country.

Our agreement with BioHEP will remain in effect until the expiration of all royalty obligations under the agreement with respect to all licensed products in all countries. We may terminate the agreement for our convenience upon 60 days' prior written notice to BioHEP. BioHEP may terminate this agreement in its entirety or on a country-by-country basis if we fail to use commercially reasonable efforts to research, develop and commercialize products in accordance with the development plan for the

licensed product. The agreement may also be terminated in its entirety or on a country-by-country basis by either party in the event of a material breach by the other party that is not cured within a specified notice period or in the case of specified bankruptcy events involving the other party.

If the agreement is terminated with respect to any one or more country, all licenses granted to us under the agreement will terminate only with respect to any such countries and specified rights in such countries will revert to BioHEP.

Manufacturing

We do not currently own or operate manufacturing facilities for production of preclinical, clinical or commercial quantities of any of our compounds or their components. To date, we have only manufactured supplies of drug substance for use in our preclinical studies at our own facilities and have contracted with several third-party contract manufacturing organizations for the supply of drug substance and finished product to meet our needs for preclinical testing, including toxicology studies and clinical trials. We believe that each of these suppliers has sufficient capacity to meet our needs, and that adequate alternative sources exist. We typically order drug substance and clinical trial supplies on a work order basis and do not enter into long-term dedicated capacity or minimum supply arrangements. However, there is a risk that, if supplies are interrupted, it would materially harm our business.

In the ordinary course of our business, we explore additional sources of supply and believe that we will have additional manufacturer(s) in place in the future for the manufacture of clinical drug supply and the commercial manufacture of inarigivir. If the supply of drug substance is insufficient to complete our trials or we are unable to obtain alternative sources of supply on favorable terms, on a timely basis or at all, our business may be adversely affected. We expect to continue to rely on third-party contract manufacturing organizations for the supply of drug substance and clinical trial supplies for our compounds for the foreseeable future.

Manufacturing is subject to extensive regulation that imposes various procedural and documentation requirements that govern record keeping, manufacturing processes and controls, personnel, quality control and quality assurance. We are reliant on our contract manufacturers to comply with these requirements, including manufacturing our compounds for use in clinical trials under current Good Manufacturing Practice, or cGMP, conditions. cGMP is a regulatory standard for the production of pharmaceuticals intended for use in humans.

Sales and Marketing

Given our stage of development, we have not yet established a commercial organization or distribution capabilities, nor have we entered into any collaboration or co-promotion arrangements. We may build focused capabilities in the United States to commercialize development programs where we believe that the medical specialists for the indications are sufficiently concentrated to allow us to promote the product effectively with a targeted sales team. We could engage in strategic relationships with biotechnology and pharmaceutical companies to accelerate the development of our programs and/or realize greater value for our shareholders due to faster access to broader geographic markets or the pursuit of broader patient populations or indications.

Competition

The development and commercialization of new drug products is highly competitive and characterized by rapid and substantial technological development and product innovations. We face competition with respect to our current product candidates and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide.

FDA-approved treatments for patients with chronic HBV include PEG-IFN-α products, including Pegasys® (PEG-IFN α-2a), marketed by Genentech, Inc., and PEG-Intron® (PEG-IFN α-2b), marketed by Merck & Co., Inc., and oral antiviral agents such as the nucleoside analog Baraclude, marketed by Bristol-Myers Squibb Company, and the nucleotide analogs Viread and Vemlidy, marketed by Gilead. In addition, several pharmaceutical and biotechnology companies, including Alnylam Pharmaceuticals, Inc., Arbutus, Arrowhead, Assembly Biosciences, Inc., Gilead and Janssen Pharmaceuticals, Inc., are developing therapies with varying mechanisms of action to address chronic HBV, including non-nucleotide antivirals and non-interferon immune enhancers. We believe that instead of competing with certain of these therapies, inarigivir has the potential to be used as a complementary therapy to certain of the treatments identified above.

There are also FDA-approved vaccinations available for children and high-risk adults that protect against HBV. These vaccines are manufactured by Merck & Co., Inc., Dynavax and GlaxoSmithKline Plc and are widely available in the United States (and less available in certain parts of the world) and have limited side effects. Although the vaccines are effective against HBV in non-infected individuals, they do not reverse or cure the disease in people who have already contracted the virus.

Our STING agonist program will face significant competition from companies in the immuno-oncology subsector of the pharmaceutical and biotechnology industry. We are aware that multiple large and small pharmaceutical companies, including Merck

& Co., Bristol-Myers Squibb Company and Novartis AG, as well as other companies such as Aduro Biotech, are actively developing potentially competitive products and technologies.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources, established presence in the market and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products 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.

We compete with the biotechnology companies listed above and others in recruiting and retaining qualified scientific, sales and marketing 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.

The key competitive factors affecting the success of inarigivir, SB 9225, SB 11285 and any other product candidates that we develop, if approved, are likely to be their efficacy, safety, convenience, price and the availability of reimbursement from government and other third-party payors.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of lower cost products.

Government Regulation and Product Approvals

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, or EU, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting and import and export of pharmaceutical products. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Review and Approval of Drugs in the United States

In the United States, the FDA approves and regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The failure to comply with requirements under the FDCA and other applicable laws 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 refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of 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.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;
- preparation and submission to the FDA of a new drug application, or NDA, requesting marketing for one or more proposed indications;

- review by an FDA advisory committee, where appropriate or if applicable;

- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;

- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;

- payment of user fees and securing FDA approval of the NDA; and

- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

Preclinical Studies

Before an applicant begins testing a compound with potential therapeutic value in humans, the drug candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as *in vitro* and animal studies to assess the potential safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to a proposed clinical trial and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA can place an IND on clinical hold at any point in development, and depending upon the scope of the hold, clinical trial(s) may not restart until resolution of the outstanding concerns to the FDA's satisfaction.

In addition, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct a continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their ClinicalTrials.gov website.

Human clinical trials are typically conducted in four sequential phases, which may overlap or be combined:

- ***Phase 1.*** The drug is initially introduced into healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.

- ***Phase 2.*** The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to evaluate preliminarily the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- ***Phase 3.*** The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to evaluate statistically the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.

- ***Phase 4***. Post-approval studies may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The FDA, the sponsor or the data monitoring committee may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When the foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain FDA regulatory requirements in order to use the study as support for an IND or application for marketing approval. Specifically, on April 28, 2008, the FDA amended its regulations governing the acceptance of foreign clinical studies not conducted under an investigational new drug application as support for an IND or a new drug application. The final rule provides that such studies must be conducted in accordance with good clinical practice, or GCP, including review and approval by an independent ethics committee, or IEC, and informed consent from subjects. The GCP requirements in the final rule encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

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

Review of an NDA by the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to an application user fee, currently exceeding $2.3 million, and the sponsor of an approved NDA is subject to annual product and establishment user fees, currently exceeding $114,000 per product and $585,000 per establishment. These fees typically increase annually. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for drugs with orphan designation and a waiver for certain small businesses.

The FDA conducts a preliminary review of an NDA generally within 60 calendar days of its receipt and strives to inform the sponsor by the 74th day after the FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs. Under that agreement, 90% of applications seeking approval of New Molecular Entities, or NMEs, are meant to be reviewed within ten months from the date on which FDA accepts the NDA for filing, and 90% of applications for NMEs that have been designated for "Priority Review" are meant to be reviewed within six months of the filing date. For applications seeking approval of drugs that are not NMEs, the ten-month and six-month review periods run from the date that FDA receives the application. The FDA may extend the review process and the Prescription Drug User Fee Act goal date for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including drug component manufacturing (e.g., active pharmaceutical ingredients), finished drug product manufacturing and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities comply with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals and elements to assure safe use, or ETASU. ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and using of patient registries. The FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product.

The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy and Priority Review Designations

The FDA is authorized to designate certain products for expedited review if the product is intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are Fast Track Designation, Breakthrough Therapy Designation and Priority Review Designation.

Specifically, the FDA may designate a product for Fast Track review if the product is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a Fast Track application does not begin until the last section of the application is submitted. In addition, the FDA may withdraw the Fast Track Designation if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, in 2012, Congress enacted the Food and Drug Administration Safety and Innovation Act, or FDASIA. This law established a new regulatory scheme allowing for expedited review of products designated as "Breakthrough Therapies." A product may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product designed to treat a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes and evidence of safety and effectiveness in a new subpopulation. A Priority Review Designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a product, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a product.

The accelerated approval pathway is most often used in settings in which the course of a disease is long, and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the product from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

The FDA's Decision on an NDA

Based on the FDA's evaluation of an NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of an NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other 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. 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 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 withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in 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, or 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 pending NDAs or supplements to approved NDAs;
- 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 found to have improperly promoted off-label uses may be subject to significant liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, and its implementing regulations, as well as the Drug Supply Chain Security Act, or DSCA, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the federal level and set minimum standards for the regulation of drug distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are "abbreviated" because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, the strength of the drug and the conditions of use of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug…"

Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity if an NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the FDASIA in 2012, sponsors must also submit pediatric study plans prior to the assessment of data. FDASIA sets forth the specific timing of the submission of the pediatric study plan. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests and any other information required by regulation. The applicant, the FDA and the FDA's internal review committee must then review the information submitted, consult with each other and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless and until the FDA promulgates a regulation stating otherwise, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application. With regard to patents, the six-month pediatric exclusivity period will not attach to any patents for which an ANDA or 505(b)(2) applicant submitted a paragraph IV patent certification, unless the NDA sponsor or patent owner first obtains a court determination that the patent if valid and infringed by the proposed product.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition, generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product. A company must request orphan drug designation before submitting an NDA for the drug and rare disease or condition. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not shorten the PDUFA goal dates for the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from the PDUFA application fee.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same indication for seven years, except in certain limited circumstances. Orphan drug exclusivity does not block the approval of a different drug for the same rare disease or condition, nor does it block the approval of the same drug for different indications. If a drug designated as an orphan drug ultimately receives marketing approval for an indication broader than

what was designated in its orphan drug application, it may not be entitled to exclusivity. Orphan drug exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same drug for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension, also known as patent term restoration, under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. Patent term extension is generally available only for drug products whose active ingredient has not previously been approved by the FDA. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the ultimate approval date. Patent term extension cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The United States PTO reviews and approves the application for any patent term extension in consultation with the FDA.

Review and Approval of Drugs in Europe and other Foreign Jurisdictions

In addition to regulations in the United States, a manufacturer is subject to a variety of regulations in foreign jurisdictions to the extent they choose to sell any drug products in those foreign countries. Even if a manufacturer obtains FDA approval of a product, it must still obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. To obtain regulatory approval of an investigational drug or biological product in the European Economic Area, or EEA, which is composed of the 28 Member States of the European Union plus Norway Iceland and Liechtenstein, a manufacturer must submit a marketing authorization application to the European Commission and EU Member State Competent Authorities. For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, clinical trials are to be conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

Clinical Trial Approval in the European Union

Pursuant to the currently applicable Clinical Trials Directive 2001/20/EC and the Directive 2005/28/EC on GCP, an applicant must obtain the approval from the competent national authority of the EU Member State in which the clinical trial is to be conducted. If the clinical trial is conducted in different EU Member States, the competent authorities in each of these EU Member States must provide their approval for the conduct of the clinical trial. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion.

In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. The new Clinical Trials Regulation will be directly applicable in and binding in all 28 EU Member States without the need for any national implementing legislation. The new Clinical Trials Regulation (EU) No 536/2014 will become applicable no earlier than 28 May 2016. It will overhaul the current system of approvals for clinical trials in the EU. Specifically, the new legislation aims at simplifying and streamlining the approval of clinical trials in the EU. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial will be required to submit a single application for approval of a clinical trial to a reporting EU Member State (RMS) through an EU Portal. The submission procedure will be the same irrespective of whether the clinical trial is to be conducted in a single EU Member State or in more than one EU Member State. The Clinical Trials Regulation also aims to streamline and simplify the rules on safety reporting for clinical trials.

Marketing Authorization

In the EEA, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA.

There are two types of MAs:

- Community MAs, which are issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use (CHMP) of the EMA and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products and medicinal products indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU. Under the Centralized Procedure, the maximum timeframe for the evaluation of a marketing authorization application is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP). Accelerated evaluation might be granted by the CHMP in exceptional cases, when the authorization of a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. Under the accelerated procedure the standard 210-day review period is reduced to 150 days.

- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned EU Member States who, within 90 days of receipt must decide whether to approve the assessment report and related materials. If a concerned EU Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the European Commission, whose decision is binding on all EU Member States.

A marketing authorization may be granted only to an applicant established in the EU. Regulation No. 1901/2006 provides that prior to obtaining a marketing authorization in the EU, an applicant must demonstrate compliance with all measures included in a Pediatric Investigation Plan, or PIP, approved by the Pediatric Committee of the EMA, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, a class waiver or a deferral for one or more of the measures included in the PIP.

Regulatory Data Exclusivity in the European Union

In the European Union, innovative medicinal products authorized in the EU on the basis of a full marketing authorization application (as opposed to an application for marketing authorization that relies on data available in the marketing authorization dossier for another, previously approved, medicinal product) are entitled to eight years of data exclusivity. During this period, applicants for authorization of generics of these innovative products cannot rely on data contained in the marketing authorization dossier submitted for the innovative medicinal product. During an additional two-year period of market exclusivity, a generic marketing authorization application can be submitted, and the innovator's data may be referenced, but no generic medicinal product can be marketed until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Periods of Authorization and Renewals in the EU

A marketing authorization is valid for five years, in principle, and it may be renewed after five years based on a reevaluation of the risk-benefit balance by the EMA or by the competent authority of the relevant EU Member State. To that end, the marketing authorization holder must provide the EMA or the relevant competent authority of the EU Member State with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the relevant competent authority of the EU Member State decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any marketing authorization that is not followed by the marketing of the medicinal product on the EU market (in the case of the centralized procedure) or on the market of the EU Member State which delivered the marketing authorization within three years after authorization ceases to be valid.

Regulatory Requirements after Marketing Authorization

Similar to the U.S., both marketing authorization holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA and the competent authorities of the individual EU Member States both before and after grant of the manufacturing and marketing authorizations.

The holder of an EU marketing authorization for a medicinal product must also comply with EU pharmacovigilance legislation and its related regulations and guidelines, which entail many requirements for conducting pharmacovigilance, or the assessment and monitoring of the safety of medicinal products. These rules can impose on central marketing authorization holders for medicinal products the obligation to conduct a labor-intensive collection of data regarding the risks and benefits of marketed products and to engage in ongoing assessments of those risks and benefits, including the possible requirement to conduct additional clinical studies.

The manufacturing process for medicinal products in the EU is highly regulated and regulators may shut down manufacturing facilities that they believe do not comply with regulations. Manufacturing requires a manufacturing authorization, and the manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU. Similarly, the distribution of medicinal products into and within the EU is subject to compliance with the applicable EU laws, regulations and guidelines, including the requirement to hold appropriate authorizations for distribution granted by the competent authorities of the EU Member States.

In the EU, the advertising and promotion of our products are subject to EU Member States' laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other legislation adopted by individual EU Member States may apply to the advertising and promotion of medicinal products. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, as approved by the competent authorities. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion. The off-label promotion of medicinal products is prohibited in the EU. The applicable laws at EU level and in the individual EU Member States also prohibit the direct-to-consumer advertising of prescription-only medicinal products. These laws may further limit or restrict the advertising and promotion of our products to the general public and may also impose limitations on our promotional activities with health care professionals.

Orphan Drug Designation and Exclusivity in the EU

Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the EU when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives the medicinal product is unlikely to be developed. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the medicinal product will be of significant benefit to those affected by that condition. Once authorized, orphan medicinal products are entitled to ten years of market exclusivity in all EU Member States and in addition a range of other benefits during the development and regulatory review process including scientific assistance for study protocols, authorization through the centralized marketing authorization procedure covering all member countries and a reduction or elimination of registration and marketing authorization fees. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the ten-year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if this product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. In addition, the period of market exclusivity may be reduced to six years if it can be demonstrated based on available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity.

Pharmaceutical Coverage, Pricing and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Even if our product candidate is approved, sales of our products will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, such products. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover our product candidate could reduce physician utilization of our products once approved and have a material adverse effect on our sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor. Third-party reimbursement and coverage may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, ensuring adequate coverage and payment for our product candidate will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of our product candidate or products to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that 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 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 product, or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states, and parallel trade, i.e., arbitrage between low-priced and high-priced member states, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products, if approved in those countries.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians and teaching physicians and patient privacy laws and regulations and other healthcare laws and regulations that may constrain our business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the United States federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing 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, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;

- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to be made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal transparency requirements known as the Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or collectively the PPACA, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Healthcare Reform

A primary trend in the United States healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, President Obama signed into law the PPACA, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of the PPACA of importance to our potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications;

- 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;

- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;

- addressed 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;

- expanded the types of entities eligible for the 340B drug discount program;

- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;

- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research;

- the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. However, the IPAB implementation has been not been clearly defined. PPACA provided that under certain circumstances, IPAB recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and

- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

Other legislative changes have been proposed and adopted in the United States since enactment of the PPACA. For example, in August 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 2012 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 up to 2% per fiscal year, which went

into effect in April 2013 and, due to the Bipartisan Budget Act of 2015, will remain in effect through 2025 unless Congress takes additional action. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several 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.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the PPACA. Congress and the current presidential administration have expressed their intentions to repeal and replace the PPACA. President Trump issued at least one Executive Order and both chambers of Congress passed bills all with the goal of fulfilling these intentions. If full or partial repeal is enacted, many if not all of the provisions of the PPACA may no longer apply to prescription drugs.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. Such reforms could have an adverse effect on anticipated revenues from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop product candidates.

Employees

As of February 28, 2019, we had 29 full-time permanent employees, of which 11 work in administration and operations and 18 work in research and development. Sixteen of our 29 full-time permanent employees hold a Ph.D. or M.D. degree. We have no collective bargaining agreements with our employees and we have not experienced any work stoppages. We consider our relations with our employees to be good.

Corporate Information

We were incorporated under the laws of the Commonwealth of Massachusetts as Spring Bank Technologies, Inc. on October 7, 2002. On May 12, 2008, we filed a certificate of incorporation in the State of Delaware and changed our state of incorporation to Delaware and our name to Spring Bank Pharmaceuticals, Inc. Our principal executive offices are located at 35 Parkwood Drive, Hopkinton, MA 01748 and our telephone number is (508) 473-5993. Our website address is www.springbankpharm.com. The information contained in, or accessible through, our website does not constitute a part of this Annual Report on Form 10-K. We make available free of charge through our website our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to these reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, as soon as reasonably practicable after we electronically file or furnish such materials to the Securities and Exchange Commission.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below in addition to the other information in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects, possibly materially. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also adversely affect our business.

Risks Related to Our Financial Position and Capital Needs

We have incurred significant losses since our inception and anticipate that we will incur significant and increasing losses in the future.

We do not have any products approved by regulatory authorities for marketing and have not generated any revenue from product sales, and we continue to incur significant research, development and other expenses related to our ongoing operations. As a result, we are not profitable and have incurred losses in every reporting period since our inception. For the years ended December 31, 2018 and 2017, we reported a net loss of $22.9 million and $27.7 million, respectively. We had an accumulated deficit of $102.1 million at December 31, 2018.

We expect to continue to incur significant and increasing losses for the foreseeable future. We anticipate these losses to increase as our expenses increase, and we expect that our expenses will increase if and as we:

- continue to develop and conduct clinical trials of our lead product candidate, inarigivir, including our ongoing Phase 2 ACHIEVE clinical trial and our upcoming Phase 2 CATALYST clinical trials of inarigivir for chronic HBV, which we refer to as the ACHIEVE trial and the CATALYST trials, respectively;
- continue preclinical development of SB 11285, our lead STING agonist product candidate, and initiate clinical trials of SB 11285, if supported by the preclinical data;
- initiate and continue research and preclinical and clinical development efforts for our other product candidates, including SB 9225, a potential fixed-dose co-formulation product that combines inarigivir and tenofovir disoproxil fumarate;
- seek to identify and develop additional product candidates;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical trials, if any;
- establish sales, marketing, distribution and other commercial infrastructure in the future to commercialize various products for which we may obtain marketing approval, if any;
- require the manufacture and supply of larger quantities of product candidates for clinical development and potentially commercialization;
- maintain, expand and protect our intellectual property portfolio;
- hire and retain additional personnel, including clinical, quality control and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and help us comply with our obligations as a public company; and
- add equipment and physical infrastructure to support our research and development programs.

We currently have no source of product revenue and may never become profitable.

Our ability to achieve and maintain profitability will depend upon our ability to generate revenue. We have not generated any revenue from product sales and do not expect to generate significant revenue unless and until we are able to gain regulatory approval of and commercialize inarigivir, SB 11285, SB 9225 or any other product candidate that we may develop, in-license or acquire in the future. Even if we are able to successfully achieve regulatory approval for any of our product candidates, we do not

know when we will generate revenue from product sales, if at all. Our ability to generate revenue from product sales of any of our product candidates also depends on a number of factors, including our ability to:

- successfully complete development activities, including filing one or more investigational new drug, or IND, applications, enrollment of trial participants and completion of the necessary clinical trials;
- enter into arrangements with third parties to further validate our technology and product candidates;
- complete and submit New Drug Applications, or NDAs, to the United States Food and Drug Administration, or FDA, and obtain regulatory approvals from the FDA for our product candidates in indications for which there is a commercial market;
- complete and submit applications to, and obtain regulatory approval from, regulatory authorities outside of the United States, or foreign regulatory authorities for our product candidates;
- successfully commercialize any approved products;
- manufacture or have manufactured commercial quantities of our products at acceptable cost levels;
- develop a commercial organization capable of manufacturing, sales, marketing and distribution for any products we intend to commercialize using internal resources;
- enter into arrangements with third parties to manufacture, market, sell and distribute our other approved products; and
- obtain adequate pricing, coverage and reimbursement from third parties for any approved products, including government and private payors.

Even if we are able to generate revenues from the sale of inarigivir, SB 11285, SB 9225 or any other product candidate, we may not generate revenues that are large enough for us to become profitable. This is in part due to the numerous risks and uncertainties associated with product development, including uncertainties regarding the timing or amount of increased expenses. Even if we are able to complete the development and regulatory process for any of our product candidates, we anticipate incurring significant costs associated with commercializing these products. Our failure to become and remain profitable would decrease the value of the Company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of product candidates or continue our operations. A decline in the value of the Company could cause you to lose all or part of your investment.

We intend to expend a significant amount of our limited resources on the development of our sole clinical stage product candidate, inarigivir, for chronic HBV, and may fail to capitalize on other technologies, product candidates or other indications that may be more profitable or for which there is a greater likelihood of success.

We are focusing a significant amount of our resources on the development of inarigivir, which concentrates the risk of product failure on one product candidate. Inarigivir may prove to be unsafe or ineffective. Because of this concentration of resources, we may forego or delay development of other technologies, product candidates or 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 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 the 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 the product candidate.

We will require additional capital to fund our operations. If we fail to obtain necessary financing, we may be forced to delay, reduce or eliminate our development and potential commercialization efforts for our product candidates.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. We expect our expenses to increase in connection with our ongoing activities, particularly as we initiate new clinical trials of, initiate new research and preclinical development efforts for and

seek marketing approval for inarigivir, SB 11285, SB 9225 and any other product candidates. Even if we obtain marketing approval for any of these product candidates, we may incur significant commercialization expenses.

We plan to continue to use our existing cash, cash equivalents and marketable securities to continue development of our product candidates, particularly inarigivir, SB 11285 and SB 9225. We expect that our cash, cash equivalents and marketable securities as of December 31, 2018 will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2021.

We will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. Adequate additional funding may not be available to us on acceptable terms or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy, and we may be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts. We do not have any committed external source of funds.

We have based our capital expenditure estimates on assumptions that may prove to be wrong, and we could deploy our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. Our future funding requirements, both near and long-term, will depend on many factors, including, but not limited to:

- initiation, progress, timing, costs and results of clinical trials evaluating inarigivir and SB 9225;
- initiation, progress, timing, costs and results of preclinical studies and, if applicable, clinical trials of SB 11285;
- initiation, progress, timing, costs and results of preclinical studies and clinical trials of any other product candidates we may develop;
- our obligation to make royalty and non-royalty sublicense payments to third-party licensors under our licensing agreements;
- the timing, receipt, and amount of milestone payments or royalties, if any, from inarigivir, SB 11285, SB 9225 or any of our other product candidates;
- the number and characteristics of product candidates that we discover or in-license and develop;
- the outcome, timing and cost of seeking regulatory review by the FDA and comparable foreign regulatory authorities, including the potential for the FDA or comparable foreign regulatory authorities to require that we perform more studies than those we currently expect;
- the costs of filing, prosecuting, defending and enforcing any patent claims and maintaining and enforcing other intellectual property rights;
- subject to receipt of marketing approval, revenue, if any, received from commercial sales of inarigivir and any other products;
- the costs and timing of the implementation of commercial-scale manufacturing activities;
- the costs and timing of establishing sales, marketing and distribution capabilities for any product candidates for which we may receive regulatory approval; and
- the costs of operating as a public company.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to inarigivir, SB 11285, SB 9225 or our other product candidates or technologies.

Until we can generate substantial revenue from product sales, if ever, we expect to seek additional capital through a combination of private and public equity offerings, debt financings, strategic collaborations and/or alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of existing stockholders may be diluted, and the terms of these securities may include provisions that adversely affect the

rights of existing stockholders. Debt financing, if available, may involve agreements that include liens or other restrictive covenants limiting our ability to take important actions, such as incurring additional debt, making capital expenditures or declaring dividends. Securing additional financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of inarigivir, SB 11285, SB 9225 and our other product candidates.

We have an effective shelf registration statement on Form S-3 (Registration No. 333-218399), or the S-3 Registration Statement, on file with the Securities and Exchange Commission pursuant to which we may, from time to time, sell up to an aggregate of $59.6 million (as of December 31, 2018) of our common stock, preferred stock, warrants, purchase rights, units, or debt securities, which includes $42.7 in shares issuable pursuant to an at-the-market offering program with Cantor Fitzgerald & Co., or Cantor, that we established in August 2017. Future sales of securities under the S-3 Registration Statement, including any sales under the at-the-market offering program, could result in dilution of our stockholders and could have a negative impact on our stock price.

If we raise additional funds through strategic collaborations and alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or grant licenses on terms that are not favorable to us, and we may be required to issue shares of our capital stock that may dilute our existing stockholders. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant rights to develop and market our technologies that we would otherwise prefer to develop and market ourselves.

We anticipate that we may need to enter into additional collaborations and relationships with strategic and development partners to develop our product candidates and market any approved products and we may be unable to attract additional collaborations with other biotechnology and pharmaceutical companies to accelerate the development of our product candidates.

We currently do not possess all of the financial and development resources necessary to develop and commercialize products that may result from our technologies. Unless we expand our product development capacity and enhance our internal marketing capability, we will need to make appropriate arrangements with strategic partners to develop and commercialize any product candidates that may be approved. A component of our business strategy includes entering into strategic collaborations and alliances or licensing arrangements with other biotechnology and pharmaceutical companies to further validate and accelerate the development of our product candidates. We may not be able to attract such partners, and even if we are able to enter into such partnerships, the terms may be less favorable than anticipated. Further, entering into partnership agreements may limit our commercialization options and/or require us to share revenues and profits with our partners, and we may have to relinquish valuable rights to our technologies or grant licenses on terms that are not favorable to us. If we are unable to enter into any of these agreements on commercially attractive terms, we may be unable to develop certain programs due to a limited availability of resources.

Risks Related to the Discovery, Development and Commercialization of Our Product Candidates

Our future success is substantially dependent on the successful clinical development, regulatory approval and commercialization of inarigivir and/or SB 9225 and will require significant capital resources and years of additional clinical development effort. If we are unable to develop, obtain regulatory approval for or successfully commercialize inarigivir or experience significant delays in doing so, our business could be materially harmed.

We do not have any products that have gained regulatory approval. As a result, our business is dependent on our ability to successfully complete clinical development of, obtain regulatory approval for, and, if approved, to successfully commercialize inarigivir and/or SB 9225 in a timely manner. The success of inarigivir and/or SB 9225 will depend on several factors, including the following:

- successful completion of our ACHIEVE trial and the successful initiation and completion of our CATALYST trials and other future trials of inarigivir;
- successful completion of additional studies to support additional clinical trials;
- initiation and successful enrollment and completion of additional clinical trials;
- safety, tolerability and efficacy profiles that are satisfactory to the FDA or any comparable foreign regulatory authority for marketing approval;
- timely receipt of marketing approvals from applicable regulatory authorities;

- the performance of our collaborators;
- establishment of supply arrangements with third-party raw materials suppliers and manufacturers;
- establishment of arrangements with third-party manufacturers to obtain finished drug products that are appropriately packaged for sale;
- obtaining and maintaining patent, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- protection of our rights in our intellectual property portfolio;
- successful launch of commercial sales following any marketing approval;
- a continued acceptable safety profile following any marketing approval;
- commercial acceptance by patients, the medical community and third-party payors following any marketing approval; and
- our ability to compete with other therapies, including therapies targeting viral hepatitis and other antiviral applications.

Many of these factors are beyond our control, including the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any collaborators. If we are unable to develop, receive marketing approval for and successfully commercialize inarigivir and/or SB 9225 or experience delays because of any of these factors or otherwise, our business could be substantially harmed.

We plan to conduct multiple clinical trials of inarigivir. If patients in any of these trials experience adverse safety events, we may be required to delay, discontinue or modify all of our clinical trials of inarigivir.

Research and development goals may not be achieved in the time frames that we publicly estimate, which could have an adverse impact on our business and could cause our stock price to decline.

We set goals, and make public statements regarding our expectations, regarding the timing of certain accomplishments, developments and milestones under our research and development programs. The actual timing of these events can vary significantly due to a number of factors, including, without limitation, the amount of time, effort and resources committed to our programs by us and any collaborators and the uncertainties inherent in the clinical development and regulatory approval process. As a result, there can be no assurance that we or any collaborators will initiate or complete clinical development activities, make regulatory submissions or receive regulatory approvals as planned or that we or any collaborators will be able to adhere to our current schedule for the achievement of key milestones under any of our programs. If we or any collaborators fail to achieve one or more of the milestones as planned, our business could be materially adversely affected, and the price of our common stock could decline.

The results of preclinical studies and clinical trials that we have conducted to date may not be predictive of results in future clinical trials.

The outcome of preclinical studies and clinical trials that we have conducted to date may not be predictive of the results of later clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical trials, even after seeing promising results in earlier preclinical studies and clinical trials. The results from our *in vitro* and *in vivo* preclinical studies may not translate into human efficacy.

We have completed a Phase 1 clinical trial of inarigivir in patients with HCV and we will complete by the end of the first quarter of 2019 a Phase 2 dose escalation trial, which we refer to as the ACHIEVE trial, in patients with chronic HBV. In the Phase 1 HCV trial, we evaluated inarigivir in 38 non-cirrhotic HCV infected patients as a monotherapy treatment for up to seven days. In the Phase 2 ACHIEVE trial, we evaluated inarigivir in 65 non-cirrhotic chronically infected HBV patients at a dose up to 200mg as a monotherapy treatment for up to twelve weeks. We expect that the dose and duration of dosing of inarigivir will be different in future clinical trials. For instance, in our planned CATALYST trials, the dose of inarigivir will increase to 400mg and the duration of the investigational therapy will be longer and involve combination therapy with other antiviral agents. As a result, our clinical trial results observed to date may not be indicative of future results in our clinical trials in patients with chronic HBV.

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 trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. If we fail to receive positive results in clinical trials of inarigivir, SB 11285 or SB 9225, the development timeline and regulatory approval and commercialization prospects for such product candidate, and, correspondingly, our business and financial prospects, would be negatively impacted.

Interim, "top-line," and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available or as additional analyses are conducted, and the data are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose interim or "top-line" from our clinical studies, which are based on a preliminary analysis of then-available efficacy, tolerability, pharmacokinetic and safety data. The results and related findings and conclusions we may draw from this top-line data are subject to change following a more comprehensive review of the data related to the particular study or trial. Interim data from clinical trials that we may complete is subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or "top-line" data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Material adverse changes between preliminary, "top-line," or interim data and final data could significantly harm our business prospects.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimations, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate and our Company in general. In addition, the information we may publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the top-line or interim data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed or delayed, which could harm our business, financial condition, operating results or prospects.

The therapeutic efficacy of inarigivir, SB 11285 and our other product candidates has not been definitively shown in humans, and we may not be able to successfully develop and commercialize inarigivir, SB 11285, SB 9225 or any of our other product candidates.

Inarigivir, SB 11285 and our other product candidates are novel compounds and their potential benefit as antiviral drugs, immunotherapies or immunomodulators, as applicable, has not been definitively shown in humans. Inarigivir, SB 11285 and our other product candidates may not prove to be effective against the indications for which they are being designed to act and may not demonstrate in future clinical trials any or all of the pharmacological effects that have been observed in preclinical studies or clinical trials to date.

Inarigivir, SB 11285, SB 9225 and our other product candidates may interact with human biological systems in unforeseen, ineffective or harmful ways. If any of our product candidates is associated with undesirable side effects or have characteristics that are unexpected, we may need to abandon the development of such product candidate or limit development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Because of these and other risks described herein that are inherent in the development of novel therapeutic agents, we may never successfully develop or commercialize inarigivir, SB 11285, SB 9225 or any of our other product candidates, in which case our business will be harmed.

Clinical development of product candidates involves a lengthy and expensive process. Additionally, there are substantial risks inherent in attempting to commercialize new drugs, and, as a result, we may not be able to successfully develop products for commercial use.

We may experience delays in our ongoing or future preclinical or clinical trials and we do not know whether planned clinical trials will begin or enroll subjects on a timely basis, need to be redesigned or be completed on schedule, if at all. Failure can occur at any time during the clinical trial process, including failure to demonstrate efficacy in a clinical trial or across a broad population of patients, the occurrence of adverse events that are severe or medically or commercially unacceptable, failure to comply with protocols or applicable regulatory requirements and determination by the FDA or any comparable foreign regulatory authority, such as the European Medicines Agency, or the EMA, that a product candidate may not continue development or is not approvable.

There can be no assurance that the FDA or other foreign regulatory authorities will not put clinical trials of inarigivir, SB 11285, SB 9225 or any of our other product candidates on clinical hold now or in the future. Clinical trials may be delayed, suspended or prematurely terminated or may take longer than anticipated for a variety of reasons, such as:

- delay or failure in reaching agreement with the FDA or a comparable foreign regulatory authority on a trial design that we are able to execute;
- delay or failure in obtaining authorization to commence a trial or inability to comply with conditions imposed by a regulatory authority regarding the scope or design of a clinical trial;
- delay or failure in reaching 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;
- delay or failure in obtaining Investigational Review Board, or IRB, approval or the approval of other reviewing entities, including comparable foreign regulatory authorities, to conduct a clinical trial at a site;
- withdrawal of clinical trial sites from our clinical trials as a result of changing standards of care or the ineligibility of a site to participate in our clinical trials;
- delay or failure in recruiting and enrolling suitable study subjects to participate in a trial;
- delay or failure in study subjects completing a trial or returning for post-treatment follow-up or otherwise complying with the trial protocol;
- clinical sites and investigators deviating from the trial protocol, failing to conduct the trial in accordance with regulatory requirements or dropping out of a trial;
- inability to identify and maintain a sufficient number of trial sites, many of which may already be engaged in other clinical trial programs, including some that may be for competing product candidates with the same indication;
- failure of our third-party service providers to satisfy their contractual duties or meet expected deadlines;
- delay or failure in adding new clinical trial sites;
- feedback from the FDA, the IRBs, data safety monitoring boards, or comparable foreign regulatory authorities, or results from earlier stage or concurrent preclinical studies and clinical trials, that might require modification of the protocol for the trial;
- decision by the FDA, the IRBs, comparable foreign regulatory authorities, or us, or recommendation by a data safety monitoring board or comparable foreign regulatory authority, to suspend or terminate clinical trials at any time for safety issues or for any other reason;
- unacceptable risk-benefit profile, unforeseen safety issues or adverse side effects or adverse events;
- failure of a product candidate to demonstrate any benefit;
- difficulties in manufacturing or obtaining from third parties sufficient quantities of a product candidate for use in clinical trials;
- lack of adequate funding to continue the clinical trial, including the incurrence of unforeseen costs due to enrollment delays, requirements to conduct additional clinical studies or increased expenses associated with the services of our CROs and other third parties; or
- changes in governmental regulations or administrative actions.

We have not yet submitted an IND application to the FDA or similar drug approval filings to any comparable foreign regulatory entity for inarigivir, SB 11285, SB 9225 or any other product candidate. We may not conduct any clinical trials for any particular product candidate in the United States until we submit an IND to the FDA for such product candidate. Because we may

develop inarigivir or SB 11285 for multiple indications, we may be required to submit multiple INDs to the FDA for these indications and may not conduct a clinical trial in the United States for that indication unless we do so.

We do not know whether any preclinical tests or clinical trials will begin as planned, will need to be restructured, or will be completed on schedule or at all. If we experience delays in any preclinical or clinical trial of our product candidates, the product candidate development and approval process could be slowed down, and as a result the costs of the development and approval process may increase, the commercial prospects of our product candidates may be harmed, and our ability to generate product revenues from these product candidates may be delayed. Significant preclinical 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 commercialize our product candidates successfully and may harm our business and results of operations. In addition, many of the factors that lead to clinical trial delays may ultimately lead to the denial of marketing approval of any of our product candidates.

If we or our collaborators experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We or our collaborators may not be able to initiate or continue clinical trials for any of our product candidates if we or our collaborators, as applicable, are unable to locate and enroll a sufficient number of eligible patients to participate in clinical trials as required by the FDA or comparable foreign regulatory authorities. Patient enrollment is a significant factor in the timing of clinical trials, and is affected by many factors, including:

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the proximity of patients to clinical sites;
- the eligibility criteria for the trial;
- the design of the clinical trial;
- efforts to facilitate timely enrollment;
- competing clinical trials; and
- clinicians' and patients' perceptions as to the potential advantages and risks 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.

For instance, in our Phase 1 clinical trial of inarigivir in patients with HCV, we experienced significant delays in enrollment due to competing clinical trials in patients with HCV being conducted by other biopharmaceutical companies, and the same could occur with respect to our planned HBV clinical trials.

Our inability to enroll a sufficient number of patients for our clinical trials could result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, delay or halt the development of and approval processes for our product candidates and jeopardize our ability to commence sales of and generate revenues from our product candidates, which could cause the value of our Company to decline.

If clinical trials of our product candidates fail to satisfactorily demonstrate safety and efficacy to the FDA and other comparable foreign regulatory authorities, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

We are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Comparable foreign regulatory authorities, such as the EMA, impose similar restrictions. We may never receive such approvals. We must complete extensive preclinical development and clinical trials to demonstrate the safety and efficacy of our product candidates in humans before we will be able to obtain these approvals.

We have never obtained marketing approval for a product candidate and we may be unable to obtain, or may be delayed in obtaining, marketing approval for any of our product candidates. Furthermore, any inability to complete preclinical and clinical

development successfully could result in additional costs to us and impair our ability to generate revenues. Moreover, if (i) we are required to conduct additional clinical trials or other testing of our product candidates beyond the trials and testing that we, or they contemplate, (ii) we are unable to successfully complete clinical trials of our product candidates or other testing, (iii) the results of these clinical trials or tests are unfavorable, uncertain or are only modestly favorable or (iv) there are unacceptable safety concerns associated with our product candidates, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;
- be subject to additional post-marketing testing or other requirements; or
- be required to remove the product from the market after obtaining marketing approval.

If we experience any of a number of possible unforeseen events in connection with clinical trials of our product candidates, potential marketing approval or commercialization of our product candidates could be delayed or prevented.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent marketing approval or commercialization of our product candidates, including:

- clinical trials of our product candidates may produce unfavorable or inconclusive results;
- we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, patient enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- the cost of planned clinical trials of our product candidates may be greater than we anticipate;
- our third-party contractors, including those manufacturing our product candidates or components or ingredients thereof or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner or at all;
- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- patients that enroll in a clinical trial may misrepresent their eligibility to do so or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the patients from the clinical trial, increase the needed enrollment size for the clinical trial or extend the clinical trial's duration;
- we may have to delay, suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their standards of conduct, a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate or findings of undesirable effects caused by a chemically or mechanistically similar product or product candidate;

- the FDA or comparable foreign regulatory authorities may disagree with our clinical trial designs or our interpretation of data from preclinical studies and clinical trials;

- the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third-party manufacturers with which we enter into agreements for clinical and commercial supplies;

- the supply or quality of raw materials or manufactured product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply; and

- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient to obtain marketing approval.

Product development costs for us will increase if we experience delays in testing or pursuing marketing approvals and we will be required to obtain additional funds to complete clinical trials and prepare for possible commercialization of our product candidates.

Inarigivir, SB 11285, SB 9225 or any other product candidate that we develop may cause undesirable side effects or have other properties that could delay or prevent its regulatory approval or limit the commercial profile of an approved label.

Undesirable side effects caused by inarigivir, SB 11285, SB 9225 or any other product candidate could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authorities.

Results of our trials could reveal an unacceptably high severity and prevalence of side effects. In such an event, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. Study drug-related side effects could affect study subject recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims.

If inarigivir, SB 11285, SB 9225 or any of our other product candidates is associated with adverse events or undesirable side effects or has properties that are unexpected, we may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause undesirable or unexpected side effects that prevented further development of the compound.

Our commercial success depends upon attaining significant market acceptance of inarigivir as a monotherapy or in combination with other antiviral agents or of any other product candidates, if approved, among physicians, patients, healthcare payors and others in the medical community necessary for commercial success, and the market opportunity for the product candidate may be smaller than we estimate.

Even if we obtain regulatory approval for inarigivir or SB 9225 or any other product candidate in chronic HBV or other indications, our product candidate may not gain market acceptance among physicians, healthcare payors, patients or the medical community. For example, physicians are often reluctant to switch their patients from existing "standard of care" therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch therapies due to lack of coverage or reimbursement for existing therapies.

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. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including the:

- efficacy and safety of our product candidates administered with other drugs each as demonstrated in clinical trials and post-marketing experience;

- clinical indications for which our product candidates are approved;

- potential and perceived advantages of our product candidates over alternative treatments;

- safety of our product candidates seen in a broader patient group, including its use outside the approved indications should physicians choose to prescribe for such uses;

- prevalence and severity of any side effects;
- product labeling or product insert requirements of the FDA or other regulatory authorities;
- timing of market introduction of our product candidates as well as of competitive products;
- cost of treatment with our product candidates in relation to alternative treatments;
- availability of coverage and adequate reimbursement and pricing by third-party payors and government authorities;
- adverse publicity about our product candidates or favorable publicity about competitive products;
- the convenience and ease of administration of our product candidates as compared to alternative treatments;
- effectiveness of our sales and marketing efforts; and
- changes in the standard of care for the targeted indications for the product candidate.

Moreover, if inarigivir or SB 9225 is approved but fails to achieve market acceptance among physicians, patients, or healthcare providers are restricted, withdrawn or recalled or fail to be approved, as the case may be, we may not be able to generate significant revenues, which would compromise our ability to become profitable.

There are also FDA-approved vaccinations available for children and high-risk adults that protect against HBV, but do not reverse or cure the disease in people who have already contracted the virus. These vaccines are manufactured by Merck & Co., Inc. and GlaxoSmithKline Plc and are widely available in the United States (and less available in certain parts of the world) and have limited side effects. If there is an increase in usage of these vaccinations, it could negatively impact the size of our addressable market.

The potential market opportunities for our product candidates are difficult to estimate precisely. Our estimates of the potential market opportunities are predicated on many assumptions, including industry knowledge and publications, third-party research reports and other surveys. While we believe that our internal assumptions are reasonable, these assumptions involve the exercise of significant judgment on the part of our management, are inherently uncertain and the reasonableness of these assumptions has not been assessed by an independent source. If any of the assumptions proves to be inaccurate, the actual markets for our product candidates could be smaller than our estimates of the potential market opportunities.

Even if we are able to commercialize inarigivir, SB 11285, SB 9225 or any other product candidate, the product candidate may not receive coverage and adequate reimbursement from third-party payors, which could harm our business.

Significant uncertainty exists as to the coverage and reimbursement status of our product candidates for which we obtain regulatory approval. Our ability to commercialize inarigivir, SB 11285, SB 9225 or any other product candidate successfully will depend, in part, on the extent to which coverage and adequate reimbursement for such product candidate will be available from third party payors, including government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, determine which medications they will cover and establish reimbursement levels.

Obtaining and maintaining adequate reimbursement for our product candidates, if approved, may be difficult. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price of a product or for establishing the reimbursement rate that such a payor will pay for the product. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and adequate reimbursement for the product. We cannot be certain if and when we will obtain an adequate level of coverage and reimbursement for our products, if they are approved, by third-party payors.

A primary trend in the United States healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. In addition, drug price transparency requirements may impact the marketing and sales of any approved products once commercialized. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical drugs. Third-party payors may also seek with respect to an approved product additional clinical evidence, beyond the data required to obtain marketing approval, demonstrating clinical benefits and value in specific patient populations or costly pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies before covering inarigivir, SB 11285 or any other product candidate. We cannot be sure that coverage and reimbursement

will be available for any of these product candidates and, if it is available, whether the level of reimbursement will be adequate. Coverage and reimbursement may impact the demand for, or the price of any of our product candidates, if approved. If reimbursement is not available or is available only at limited levels, we may not be able to commercialize inarigivir, SB 11285 or any other product candidate successfully, if approved.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may only be temporary. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to obtain coverage and profitable reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

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

The development and commercialization of new drug products is highly competitive in our therapeutic areas of interest. We expect that we will face competition with respect to inarigivir, SB 11285, SB 9225 and any other product candidates that we may seek to develop or commercialize, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. For instance, there are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of chronic HBV. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

We expect inarigivir and SB 9225 to face intense and increasing competition as new products enter the relevant antiviral markets and advanced technologies become available. FDA-approved treatments for patients with chronic HBV include pegylated interferon-α, or PEG-IFN-α, products including Pegasys (PEG-IFN α-2a), marketed by Genentech, Inc., and PEG-Intron (PEG-IFN α-2b), marketed by Merck & Co., Inc., or Merck, and oral antiviral agents such as the nucleoside analog Baraclude (entecavir), marketed by Bristol-Myers Squibb Company, or BMS, and the nucleotide analogs Viread (tenofovir disoproxil fumarate) and Vemlidy (tenofovir alafenamide), both marketed by Gilead Sciences, Inc. These treatments are designed to decrease the risk of liver damage from chronic HBV by slowing down or stopping the virus from reproducing. In addition, several pharmaceutical and biotechnology companies, including Alnylam Pharmaceuticals, Inc., Arbutus Biopharma Corp., Arrowhead Research Corporation, or Arrowhead, Assembly Biosciences, Inc., Gilead Sciences, Inc. and Janssen Pharmaceuticals, Inc., are developing therapies with varying mechanisms of action to address chronic HBV, including non-nucleotide antivirals and non-interferon immune enhancers.

There are a variety of available antiviral therapies and supportive care products for viral diseases. Some of these other drugs are branded and subject to patent protection, some are in clinical development and not yet approved, and others are available on a generic basis. Many of the approved drugs are well-established therapies or products and are widely accepted by physicians, patients and third-party payors. Insurers and other third-party payors may also encourage the use of generic products. These factors may make it difficult for us to achieve market acceptance at desired levels and/or in a timely manner to ensure viability of our business.

We also expect our STING agonist program, including SB 11285, to face intense and increasing competition from companies in the immuno-oncology subsector of the pharmaceutical and biotechnology industry. Specifically, Merck and Aduro Biotech, Inc. recently disclosed early clinical trial results relating to their STING agonist programs. We are also aware of multiple small and large pharmaceutical and biotechnology companies, including Novartis AG, GlaxoSmithKline plc and BMS, that have STING agonist programs.

Many of our existing and potential future competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining marketing approvals and marketing approved products than we do.

Our competitors may obtain regulatory approval of their products before we are able to, which may limit our ability to develop or commercialize inarigivir, SB 11285, SB 9225 or any of our other product candidates. Our competitors may also develop drugs that are safer, more effective, more convenient or less expensive than ours, and may also be more successful than us in manufacturing and marketing their products. In addition, our competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective, have fewer or more tolerable side effects or are less costly than any product candidates that we are currently developing or that we may develop. These appreciable advantages could reduce or eliminate our commercial opportunity and render inarigivir, SB 11285, SB 9225 or any other product candidates obsolete or non-competitive.

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 and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. For instance, in October 2018, Janssen Pharmaceuticals announced that it had entered into a worldwide license agreement with Arrowhead to develop and commercialize Arrowhead's HBV candidate, a Phase 1/2 subcutaneous, ribonucleic acid interference (RNAi) therapy candidate being investigated for the treatment of HBV. These third parties compete with us in recruiting and retaining qualified scientific, management and commercial personnel, establishing clinical trial sites and subject registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of inarigivir, SB 11285, SB 9225 or any other product candidates.

We face an inherent risk of product liability exposure related to the testing of our product candidates by us or our investigators in human clinical trials and will face an even greater risk if we commercially sell inarigivir, SB 11285, SB 9225 or any of our other product candidates if and after we obtain regulatory approval. Product liability claims may be brought against us by study subjects enrolled in our clinical trials, patients, healthcare providers or others using, administering or selling inarigivir, SB 11285, SB 9225 or any of our other product candidates. If we cannot successfully defend ourselves against claims that our product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in, for example:

- decreased demand for inarigivir, SB 11285, SB 9225 or any of our other product candidates;
- the inability to commercialize these product candidates;
- termination of clinical trial sites or entire trial programs;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial subjects;
- significant costs to defend the related litigation;
- substantial monetary awards to clinical trial subjects or patients;
- loss of revenue;
- diversion of management and scientific resources from our business operations; and
- increased scrutiny and potential investigation by, among others, the FDA, the United States Department of Justice, or DOJ, the Office of Inspector General of the office of Health and Human Services, or HHS, state attorneys general, members of Congress and the public.

Failure in our or our vendors' information technology and storage systems, including data breaches subject to the new General Data Protection Regulation in the European Union, could significantly disrupt the operation of our business.

Our ability to execute our business plan and maintain operations depends on the continued and uninterrupted performance of our information technology and storage systems. Our internal computer systems may be vulnerable to risks and damages from a variety of sources, including telecommunications or network failures, malicious human acts and natural disasters. Moreover, despite the implementation of network security and back-up measures, some of our and our vendors' servers are potentially vulnerable to physical or electronic break-ins, computer viruses and similar disruptive problems. Our systems may safeguard important confidential personal data regarding our subjects. If a disruption event were to occur and cause interruptions in our operations, it could result in a

material disruption of our drug development programs. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

In addition, data security breaches, whether by employees or others, may expose sensitive data to unauthorized persons. Effective May 25, 2018, the European Union implemented the General Data Protection Regulation, or GDPR, a broad data protection framework that expanded the scope of European Union data protection law to non-European Union entities that process, or control the processing of, the personal information of European Union subjects, including clinical trial data. The GDPR allows for the imposition of fines and/or corrective action on entities that improperly use or disclose the personal information of European Union subjects, including through a data security breach. Accordingly, data security breaches experienced by us, our collaborators or contractors could lead to significant fines, required corrective action, loss of trade secrets or other intellectual property, or could lead to the public exposure of personally identifiable information (including sensitive personal information) of our employees, collaborators, clinical trial patients, and others. A data security breach or privacy violation that leads to disclosure or modification of or prevents access to patient information, including personally identifiable information or protected health information, could harm our reputation, compel us to comply with breach notification laws, subject us to mandatory corrective action, require us to verify the correctness of database contents and otherwise subject us to liability under laws and regulations that protect personal data, resulting in increased costs or loss of revenue. The GDPR imposes several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, the security and confidentiality of the personal data, data breach notification and the use of third-party processors in connection with the processing of personal data. The GDPR also imposes strict rules on the transfer of personal data out of the European Union to the United States and provides an enforcement authority to impose large penalties for noncompliance, including the potential for fines of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. The GDPR increases our responsibility and liability in relation to personal data that we process, including in clinical trials, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, which could divert management's attention and increase our cost of doing business. If we are unable to prevent such data security breaches or privacy violations or implement satisfactory remedial measures, our operations could be disrupted, and we may suffer loss of reputation, financial loss and other regulatory penalties because of lost or misappropriated information, including sensitive patient data. In addition, these breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. Moreover, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information, trade secrets or other intellectual property. While we have implemented security measures to protect our data security and information technology systems, such measures may not prevent such events.

Despite precautionary measures to prevent unanticipated problems, including data breaches, that could affect our technology systems, sustained or repeated system failures that interrupt our ability to generate and maintain data could adversely affect our ability to operate our business.

Business disruptions could seriously harm our future revenues and financial condition and increase our costs and expenses.

Our operations could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or man-made disasters or business interruptions, for which we are predominantly self-insured. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

We rely on third-party manufacturers to produce inarigivir and expect to rely on third-party manufacturers to produce our other product candidates in the future. Our ability to obtain clinical supplies of inarigivir or other product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption. The ultimate impact on us, our significant suppliers and our general infrastructure of being in certain geographical areas is unknown, but our operations and financial condition could suffer in the event of a major earthquake, fire or other natural disaster.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines or their relationship with us is terminated, our business may be harmed and our drug development efforts could be delayed.

We rely on third-party research vendors, academic research institutions, CROs, and other third parties to conduct and provide us with significant data and other information related to our projects, preclinical studies and clinical trials. We rely on these parties for execution of our preclinical studies and clinical trials, and we control only some aspects of their activities. If these third

parties provide inaccurate, misleading, or incomplete data, our business, prospects, and results of operations could be materially adversely affected. Nevertheless, we are responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities. We also rely on third parties to assist in conducting our preclinical studies in accordance with good laboratory practice, or GLP, and the Animal Welfare Act requirements. We and our service providers are required to comply with federal regulations and good clinical practice or GCP, which are international standards meant to protect the rights and health of subjects that are enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities. Regulatory authorities enforce GCP through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our service providers fail to comply with applicable GCP, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot guarantee that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements. In addition, our clinical trials must be conducted with product produced under current Good Manufacturing Practices, or cGMPs. Failure to comply with these regulations may require us to repeat preclinical studies and clinical trials, which would delay the regulatory approval process.

Our service providers are not our employees, and except for remedies available to us under our agreements with such service providers, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical, nonclinical and preclinical programs. If service providers do not successfully carry out their contractual duties or obligations or meet expected deadlines or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our protocols, regulatory requirements or for other reasons, our preclinical studies and clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize inarigivir, SB 9225, SB 11285 or any of our other product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Because we have relied and continue to rely on third parties, our internal capacity to perform these functions is limited. Outsourcing these functions involves risk that third parties may not perform to our standards, may not produce results in a timely manner or may fail to perform at all. In addition, the use of third-party service providers requires us to disclose our proprietary information to these parties, which could increase the risk that this information will be misappropriated. We currently have a small number of employees, which limits the internal resources we have available to identify and monitor our third-party providers. To the extent we are unable to identify and successfully manage the performance of third-party service providers in the future, our business may be adversely affected. Though we carefully manage our relationships with our service providers, 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 material adverse impact on our business, financial condition and prospects.

Our third-party vendors and service providers generally have the right to terminate their agreements with us under certain circumstances. Identifying, qualifying and managing performance of third-party service providers can be difficult, time consuming and cause delays in our development programs. In addition, there is a natural transition period when a new third-party vendor or service provider commences work, and the new third-party vendor or service provider may not provide the same type or level of services as the original provider. If any of our relationships with our third-party vendors or service providers terminate, we may not be able to enter into arrangements with alternative third-party vendors or service providers or to do so on commercially reasonable terms.

We have no experience manufacturing any product candidate on a commercial scale and have no manufacturing facility. We are dependent on contract manufacturers for the manufacture of inarigivir, SB 11285 and SB 9225 as well as on third parties for our supply chain and expect to rely on contract manufacturers for any other product candidates. If we experience problems with any such contract manufacturers, the manufacturing of inarigivir, SB 11285, SB 9225 or any other product candidate could be delayed.

We currently have no manufacturing facilities and limited personnel with manufacturing experience. We rely on contract manufacturers to produce both drug substance and drug product required for our clinical trials. We plan to continue to rely upon contract manufacturers to manufacture commercial quantities of our products, if approved. Reliance on such third-party contractors entails risks, including:

- delays by our third-party contract manufacturers to produce and deliver sufficient supply of clinical trial materials, including but not limited to third-party contractors giving greater priority to the supply of other products over our product candidates or otherwise not satisfactorily performing according to the terms of the agreements between us and them;
- the possible termination or nonrenewal of agreements by our third-party contractors at a time that is costly or inconvenient for us;

- the possible breach by the third-party contractors of our agreements with them;
- the failure of third-party contractors to comply with applicable regulatory requirements;
- the possible mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;
- the possibility of clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

We currently rely, and expect to continue to rely, on a small number of third-party contract manufacturers to supply the majority of our active pharmaceutical ingredient, or API, and required finished product for our preclinical studies and clinical trials. These contract manufacturers are typically single source suppliers to us. We do not have long-term agreements with any of these third parties. If any of our existing manufacturers become unavailable to us for any reason, we may experience a delay in identifying or qualifying replacements.

For instance, in 2016, we had to transition the manufacture of the drug substance for inarigivir to another supplier. While we currently believe we will have sufficient drug substance to complete our Phase 2 clinical trials of inarigivir for chronic HBV, if the supply of drug substance turns out to be insufficient to complete such trials or we are unable to obtain alternative sources of supply on favorable terms, on a timely basis or at all, our business may be adversely affected.

Each of our API and drug product manufacturers must comply with cGMPs and other stringent regulatory requirements enforced by the FDA and foreign regulatory authorities in other jurisdictions. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation, which occur in addition to our own quality assurance releases. Manufacturers of our products may be unable to comply with these GMP requirements and with other regulatory requirements. We have little control over our manufacturers' or partners' compliance with these regulations and standards.

Any manufacturing problem or the loss of a contract manufacturer could be disruptive to our operations, delay our clinical trials and, if any of our products are approved for sale, result in lost sales. Our manufacturers may experience problems with their respective manufacturing and distribution operations and processes, including for example, quality issues, such as product specification and stability failures, procedural deviations, improper equipment installation or operation, utility failures, contamination and natural disasters. In addition, the raw materials necessary to make API for our products are acquired from a limited number of sources. Any delay or disruption in the availability of these raw materials or a change in raw material suppliers could result in production disruptions, delays or higher costs with consequent adverse effects on us. Any reliance on suppliers may involve additional risks, including a potential inability to obtain critical materials and reduced control over production costs, delivery schedules, reliability and quality. Any unanticipated disruption to future contract manufacture caused by problems at suppliers could delay shipment of our product candidates, increase our cost of goods sold or, if any of our products are approved for sale, result in lost sales.

If any of our product candidates are approved by any regulatory agency, we plan to enter into agreements with third-party contract manufacturers for the commercial production and distribution of those products. It may be difficult for us to reach agreement with a contract manufacturer on satisfactory terms or in a timely manner. In addition, we may face competition for access to manufacturing facilities, as there are a limited number of contract manufacturers operating under cGMPs that are capable of manufacturing our product candidates. Consequently, we may not be able to reach agreement with third-party manufacturers on satisfactory terms, which could delay our commercialization efforts.

Third-party manufacturers are required to comply with cGMPs and similar regulatory requirements outside the United States. Facilities used by our third-party manufacturers must be approved by the FDA after we submit an NDA and before potential approval of the product candidate. Similar regulations apply to manufacturers of our product candidates for use or sale in foreign countries. We do not control the manufacturing process and are completely dependent on our third-party manufacturers for compliance with the applicable regulatory requirements for the manufacture of our product candidates. If our manufacturers cannot successfully manufacture material that conforms to our specifications or the strict regulatory requirements of the FDA and any applicable foreign regulatory authority, they will not be able to secure the applicable approval for their manufacturing facilities. If these facilities are not approved for commercial manufacture, we may need to find alternative manufacturing facilities, which could result in delays in obtaining approval for the applicable product candidate.

In addition, our manufacturers are subject to ongoing periodic inspections by the FDA and corresponding state and foreign agencies for compliance with cGMPs and similar regulatory requirements both prior to and following the receipt of marketing approval for any of our product candidates. Some of these inspections may be unannounced. Failure by any of our manufacturers to comply with applicable cGMPs or other regulatory requirements could result in sanctions being imposed on us, including fines,

injunctions, civil penalties, delays, suspensions or withdrawals of approvals, operating restrictions, interruptions in supply and criminal prosecutions, any of which could adversely affect supplies of our product candidates and significantly harm our business, financial condition and results of operations.

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

If we enter into additional licensing or collaboration agreements with third parties to develop, obtain regulatory approvals for and commercialize inarigivir, SB 11285 or any other product candidates, our prospects with respect to those product candidates will depend in significant part on the success of those collaborations.

We are a party to preclinical and clinical collaborations with third parties to evaluate the combination of our product candidates and the third party's product candidate, including our ACHIEVE trial being conducted under our clinical trial supply and collaboration with Gilead. We expect to enter into additional collaborations with other pharmaceutical or biotechnology companies in developing our product candidates, including inarigivir, SB 11285 and our other product candidates. Under such collaborations, we have or may have limited control over the amount and timing of resources that our collaborators will dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will, in part, depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, in the case of collaborations intended to evaluate the combination of inarigivir, SB 11285 and other product candidates, the success of any such collaboration may depend on the success of the development of the product or product candidate that our collaborator is developing. For instance, in the event that any of these third parties have unforeseen issues that negatively impact their clinical development or marketing approval for their products or product candidates or otherwise negatively affect their ability to continue to clinically develop or market their products or product candidates, our ability to complete our applicable clinical trials and/or evaluate clinical results and, ultimately, our ability to receive regulatory approval for our product candidates for the indications we are pursuing may also be negatively impacted.

Collaborations involving our product candidates pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will devote to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of our product candidates 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 a clinical trial program, 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;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might 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;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If any future collaborator of ours is involved in a business combination, it could decide to delay, diminish or terminate the development or commercialization of any product candidate licensed to it by us.

Despite our efforts, we may be unable to secure additional collaborative licensing or other arrangements that are necessary for us to further develop and commercialize inarigivir, SB 11285, SB 9225 or any other product candidates. We face significant competition in seeking appropriate collaborators. 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 potential differentiation of our product candidate from competing product candidates, design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities and the regulatory pathway for any such approval, the potential market for the product candidate, the costs and complexities of manufacturing and delivering the product to patients and the potential of competing products. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available for collaboration and whether such a collaboration could be more attractive than the one with us for our product candidate. Supporting diligence activities conducted by potential collaborators and negotiating the financial and other terms of a collaboration agreement are long and complex processes with uncertain results. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

Risks Related to Regulatory Approval and Marketing of Our Product Candidates and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time consuming and uncertain and may prevent us or any future collaborators from obtaining approvals for the commercialization of inarigivir, SB 11285, SB 9225 or our other product candidates. As a result, we cannot predict when or if, and in which territories, we, or any future collaborators, will obtain marketing approval to commercialize inarigivir, SB 11285, SB 9225 or our other product candidates.

The research, testing, manufacturing, labeling, approval, selling, marketing, promotion and distribution of products are subject to extensive regulation by the FDA and comparable foreign regulatory authorities. We, and any future collaborators, are not permitted to market any of our product candidates in the United States or in other countries until we, or they, receive approval of an NDA from the FDA or marketing approval from applicable foreign regulatory authorities. Product candidates in various stages of development are subject to the risks of failure inherent in drug development. We have not submitted an application for or received marketing approval for inarigivir, SB 11285 or any of our product candidates in the United States or in any other jurisdiction. We have limited experience in conducting and managing the clinical trials necessary to obtain marketing approvals, including FDA approval of an NDA.

The process of obtaining marketing approvals, both in the United States and abroad, is lengthy, expensive and uncertain. It may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. The FDA or other regulatory authorities may determine that inarigivir, SB 11285, SB 9225 and our other product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude us from obtaining marketing approval or prevent or limit commercial use. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

In addition, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. For example, on June 23, 2016, eligible members of the electorate in the United Kingdom decided by referendum to leave the European Union, commonly referred to as "Brexit". On March 29, 2017, the United Kingdom formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty.

Because a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially change the regulatory regime applicable to the approval of any of our product candidates in the United Kingdom. In addition, because the European Medicines Agency, or EMA, is currently located in the United Kingdom but expected to move to the Netherlands as a result of Brexit, the implications for the regulatory review process in the European Union has not been fully clarified and could result in disruption to the EMA review process.

Reasons that the FDA or comparable foreign regulatory authorities may not approve our product candidates, include:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Any delay in obtaining or failure to obtain required approvals could negatively affect our ability or that of any future collaborators to generate revenue from the particular product candidate, which likely would result in significant harm to our financial position and adversely impact our stock price.

A Breakthrough Therapy Designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval.

We do not currently have Breakthrough Therapy Designation for any of our product candidates but may seek such designation. A Breakthrough Therapy Designation may be granted to a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and for which preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as Breakthrough Therapies, interaction and communication between the FDA and the sponsor can help to identify the most efficient path for development. Drugs designated as Breakthrough Therapies are also eligible for accelerated approval.

Designation as a Breakthrough Therapy is within the discretion of the FDA. Accordingly, even if we believe, after completing early clinical trials, that one of our product candidates meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead determine not to grant such designation. In any event, the receipt of a Breakthrough Therapy designation by itself for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as a Breakthrough Therapy, the FDA may later decide that such product candidates no longer meet the conditions for qualification.

A Fast Track Designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process and does not increase the likelihood that our product candidates will receive marketing approval.

We do not currently have Fast Track Designation for any of our product candidates but may seek such designation. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA Fast Track Designation. The FDA has broad discretion whether to grant this designation. Even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program. Many drugs that have received Fast Track Designation have failed to obtain drug approval.

Failure to obtain marketing approval in foreign jurisdictions would prevent inarigivir, SB 11285, SB 9225 or any other product candidate from being marketed abroad. Any approval we are granted in the United States would not assure approval in foreign jurisdictions.

In order to market and sell our products in the European Union and other foreign jurisdictions, including Japan, China and South Korea, we, and any future collaborators, must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The marketing approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, a product must be approved for reimbursement before the product can be approved for sale in that country. We, and any future collaborators, may not obtain approvals from foreign regulatory authorities on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may file for marketing approvals but not receive necessary approvals to commercialize our products in any market. If we are unable to obtain approval of our product candidates by regulatory authorities in the European Union, Japan, China, South Korea or another foreign country or jurisdiction, the commercial prospects of our product candidates may be significantly diminished, and our business prospects could decline.

Any of our product candidates for which we, or any future collaborators, obtain marketing approval in the future could be subject to post-marketing restrictions or withdrawal from the market and we, or any future collaborators, may be subject to substantial penalties if we, or they, fail to comply with regulatory requirements or if we, or they, experience unanticipated problems with our products following approval.

Any of our product candidates for which we, or any future collaborators, obtain marketing approval, as well as the manufacturing processes, post-approval studies and measures, labeling, advertising and promotional activities for such product, among other things, will be subject to ongoing requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Thus, even if marketing approval of inarigivir or another product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a Risk Evaluation and Mitigation Strategy.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product. The FDA and other agencies, including the Department of Justice, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we, or any future collaborators, do not market any of our product candidates for which we, or they, receive marketing approval for only their approved indications, we, or they, may be subject to warnings or enforcement action for off-label marketing. Similar post-market requirements may apply in foreign jurisdictions in which we may seek approval of our products. Violation of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws.

In addition, the holder of an approved NDA is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the NDA. Later discovery of previously unknown adverse events or other problems with our products or their manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;

- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters asserting that we are in violation of the law;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- restrictions on coverage by third-party payors;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of products;
- product seizure;
- refusal to permit us to enter into government contracts; or
- injunctions or the imposition of civil or criminal penalties.

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

We are subject to healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, fines, disgorgement, exclusion from participation in government healthcare programs, curtailment or restricting of our operations, and diminished profits and future earnings.

Healthcare providers, physicians and others will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our future arrangements with healthcare providers, patients and third-party payors will expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. Restrictions under applicable US federal and state healthcare laws and regulations include the following:

Anti-Kickback Statute. The federal healthcare Anti-Kickback Statute prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, 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 federal healthcare programs, such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the Anti-Kickback Statute or specific intent to violate it in order to have committed a violation;

False Claims Laws. Federal civil and criminal false claims laws and civil monetary penalties laws, including the federal False Claims Act, 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 federal government claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;

HIPAA. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or for making any false statements relating to healthcare matters. Similar to the Federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate the statute in order to have committed a violation. Additionally, HIPAA, as amended by HITECH and its implementing regulations, imposes obligations on certain covered entities as well as their business associates that perform certain services involving the use or

disclosure of individually identifiable health information, including mandatory contractual terms with respect to safeguarding the privacy, security and transmission of individually identifiable health information, and require notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information;

Privacy Regulations and the GDPR. Privacy and data security have become significant issues in the United States, Europe and in many other jurisdictions where we may in the future conduct our operations. Regulators globally are imposing greater monetary fines for privacy violations. For example, in 2016, the European Union adopted the GDPR, which became effective on May 25, 2018. The GDPR applies to any company established in the European Union as well as to those outside the European Union if they collect and use personal data in connection with the offering goods or services to individuals in the European Union or the monitoring of their behavior. The GDPR enhances data protection obligations for processors and controllers of personal data, including, for example, expanded disclosures about how personal information is to be used, limitations on retention of information, mandatory data breach notification requirements and onerous new obligations on services providers. Non-compliance with the GDPR may result in monetary penalties of up to €20 million or 4% of worldwide revenue, whichever is higher. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of personal data, such as healthcare data or other sensitive information, could greatly increase our cost of providing our products and services or even prevent us from offering certain services in jurisdictions that we may operate in.

Transparency Requirements. The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the Department of Health and Human Services 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;

FDCA. The federal Food, Drug and Cosmetic Act, or FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices; and

Analogous State and Foreign Laws. Analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, and transparency laws, may apply to sales or marketing arrangements, and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers. In addition, some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties, and our business generally, will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations 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 these laws or any other governmental laws and regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, contractual damages, reputational harm, disgorgement, curtailment or restricting of our operations, any of which could substantially disrupt our operations and diminish our profits and future earnings. If any of the physicians or other providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available under such laws, it is possible that some of our business activities, including our relationships with physicians and other healthcare providers, some of whom will recommend, purchase and/or prescribe our products, could be subject to challenge under one or more of such laws.

Current and future legislation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of inarigivir, SB 11285, SB 9225 or our other product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any future collaborators, to profitably sell any products for which we, or they, obtain marketing approval. We expect that current laws,

as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for any approved products.

For example, in March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the PPACA. Among the provisions of the PPACA of potential importance to our business and our product candidates are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate 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 healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- 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;
- extension of manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- a new Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs; and
- establishment of the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and, due to subsequent legislation, will continue until 2025, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Some of the provisions of the PPACA have yet to be implemented, and there have been legal and political challenges to certain aspects of the PPACA. Since January 2017, President Trump has signed two executive orders and other directives designed to delay, circumvent, or loosen certain requirements mandated by the PPACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the PPACA. While Congress has not passed repeal legislation, the JOBS Act includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". Congress may consider other legislation to repeal or replace elements of the PPACA. Many of the details regarding the implementation of the PPACA are yet to be determined, and at this time, the full effect that the PPACA would have on a pharmaceutical manufacturer remains unclear. We cannot predict the full impact of the PPACA or future reform measures on our operations. However, any reduction in reimbursement from Medicare or other government programs may result in a similar reduction

in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. The Budget Control Act of 2011, the American Taxpayer Relief Act of 2012, and a repeal or partial repeal and replacement of the PPACA may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which regulatory approval is obtained.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the United States Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and any future collaborators to more stringent product labeling and post-marketing testing and other requirements. If we are not able to achieve and maintain regulatory compliance, we may not be permitted to market our products and/or product candidates, which would adversely affect our ability to generate revenue and achieve or maintain profitability.

We have international operations and conduct clinical trials outside of the United States. A number of risks associated with international operations could materially and adversely affect our business.

We have conducted clinical trials in Canada, Australia and New Zealand, and certain Asian jurisdictions, and we anticipate that we will soon conduct clinical trials in additional jurisdictions, primarily in the European Union and Asia. Accordingly, we are subject to risks associated with doing business globally, including commercial, political, and financial risks. Emerging regions, such as Eastern Europe and Asia, as well as more developed markets, such as the United Kingdom, France, Germany, and Australia, provide clinical study opportunities for us. In addition, we are subject to potential disruption caused by military conflicts; potentially unstable governments or legal systems; civil or political upheaval or unrest; local labor policies and conditions; possible expropriation, nationalization, or confiscation of assets; problems with repatriation of foreign earnings; economic or trade sanctions; closure of markets to imports; anti-American sentiment; terrorism or other types of violence in or outside the United States; health pandemics; and a significant reduction in global travel. Our success will depend, in part, on our ability to overcome the challenges we encounter with respect to these risks and other factors affecting U.S. companies with global operations. If our global clinical trials were to experience significant disruption due to these risks or for other reasons, it could have a material adverse effect on our financial results.

Beyond conducting our clinical trials outside of the U.S., we also expect to be subject to a number of risks related with our international operations, many of which may be beyond our control. These risks include:

- different standards of care in various countries that could complicate the evaluation of our product candidates;
- different U.S. and foreign drug import and export rules;
- different reimbursement systems and different competitive drugs indicated to treat the indication for which our product candidates are being developed;
- reduced protection for intellectual property rights in certain countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- foreign currency fluctuations and compliance with foreign currency exchange rules, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country; and
- business interruptions resulting from geopolitical actions, including tariffs, war and terrorism, or natural disasters.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain 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 dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. For instance, the FCPA prohibits any United States individual or business from paying, offering, 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 certain accounting provisions requiring maintenance of books and records that accurately and fairly reflect all transactions of the company, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, the government operates hospitals, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and 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 Securities and Exchange Commission also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, but this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for any environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Our employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of fraud, misconduct or other illegal activity by our employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with federal and state data privacy, security, fraud and abuse and other healthcare laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. 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, incentive programs and other business arrangements.

Misconduct could also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creating fraudulent data in our preclinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and serious harm to our reputation. 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, standards or regulations. Additionally, we are subject to the risk that a person or government agency 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 and results of operations, including the imposition of significant fines or other sanctions.

Inadequate funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, most recently in December 2018, the U.S. government shut down several times and certain regulatory agencies, including the FDA and the SEC, had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown again occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Risks Related to Our Intellectual Property

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

We are a party to a license agreement with BioHEP Technologies Ltd. (formerly known as Micrologix Biotech, Inc.), or BioHEP, under which we license certain patents and know-how to make, have made, use, sell, offer to sell and import certain product candidates, including inarigivir. We may enter into additional license agreements in the future. Our license agreement with BioHEP imposes, and we expect that future license agreements will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with our obligations under these licenses, our licensors may have the right to terminate these license agreements, in which event we might not be able to market any product that is covered by these agreements, which could materially adversely affect the value of the product candidate being developed under the license agreement. Termination of these license agreements may result in our having to negotiate new or reinstated licenses with less favorable terms.

If we are unable to protect our intellectual property rights or if our intellectual property rights are inadequate for our technology and product candidates, our competitive position could be harmed.

Our success will depend in large part on our ability to obtain and maintain patent and other intellectual property protection in the United States and other countries with respect to our proprietary technology and product candidates. We rely on trade secret, patent, copyright and trademark laws, and confidentiality, licensing and other agreements with employees and third parties. We seek to protect our proprietary position by filing and prosecuting patent applications in the United States and abroad related to our novel technologies and product candidates that are important to our business.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development before it is too late to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development, such as our employees, strategic partners, consultants, advisors and other third parties, any of these parties may breach the agreements and disclose our confidential information before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

We may license patent rights that are valuable to our business from third parties, in which event we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology or medicines underlying such licenses. We cannot be certain that these patents and applications will be prosecuted and enforced in a manner

consistent with the best interests of our business. If any such licensor fails to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated and our right to develop and commercialize any of our product candidates that are the subject of such licensed rights could be adversely affected. In addition to the foregoing, the risks associated with patent rights that we license from third parties also apply to patent rights we own.

The patent positions of biotechnology and pharmaceutical companies generally are highly uncertain, involve complex legal and factual questions and have in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patents, including those patent rights licensed to us by third parties, are highly uncertain. The steps we or our licensors have taken to protect our proprietary rights may not be adequate to preclude misappropriation of our proprietary information or infringement of our intellectual property rights, both inside and outside the United States. Further, the examination process may require us or our licensors to narrow the claims for our pending patent applications, which may limit the scope of patent protection that may be obtained if these applications issue as patents. The rights already granted under any of our currently issued patents or those licensed to us and those that may be granted under future issued patents may not provide us with the proprietary protection or competitive advantages we are seeking. Changes in the patent laws, implementing regulations or interpretation of the patent laws in the United States and other countries may also diminish the value of our patents or narrow the scope of our patent protection. If we or our licensors 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 sufficient, our competitors could develop and commercialize technology and products similar or superior to ours, and our ability to successfully commercialize our technology and product candidates may be adversely affected.

With respect to patent rights, we do not know whether any of the pending patent applications for any of our compounds will result in the issuance of patents that protect our technology or products, or if any of our or our licensors' issued patents will effectively prevent others from commercializing competitive technologies and products. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or in some cases not at all, until they are issued as a patent. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions.

Our pending applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Because the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, issued patents that we own or have licensed from third parties may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in the loss of patent protection, the narrowing of claims in such patents or the invalidity or unenforceability of such patents, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection for our technology and products. Protecting against the unauthorized use of our or our licensors' patented technology, trademarks and other intellectual property rights is expensive, difficult and in some cases may not be possible. In some cases, it may be difficult or impossible to detect third-party infringement or misappropriation of our intellectual property rights, even in relation to issued patent claims, and proving any such infringement may be even more difficult.

If third parties initiate legal proceedings against us alleging that we are infringing their intellectual property rights, such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing our product candidates.

Our commercial success depends upon our ability to develop, manufacture, market and sell inarigivir, SB 11285, SB 9225 and any other product candidates and to use our related proprietary technologies, without infringing the intellectual property and other proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, and interferences, post-grant review, inter partes review, and reexamination proceedings before the United States Patent and Trademark Office, or USPTO, and corresponding foreign patent offices. As a result, we may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to inarigivir, SB 11285, SB 9225 or any other product candidates, including interference or derivation proceedings before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. The pharmaceutical and biotechnology industries have produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods of treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications, which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed

during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product unless we obtained a license under the applicable patents, or until such patents expire. Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product candidate.

If we were sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Under certain circumstances, we could be forced, including by court order, to cease commercializing the applicable product candidate. In addition, in any such proceeding or litigation, we could be found liable for monetary damages. A finding of infringement could prevent us from commercializing the applicable product candidate or force us to cease some of our business operations, which could materially harm our business.

Defense of claims of infringement, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. 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. Parties making claims against us may also obtain injunctive or other equitable relief, which could effectively block our ability to develop and commercialize one or more of our product candidates, which could materially harm our business.

Most of our competitors are larger than we are and have substantially greater resources and may be able to sustain the costs of complex patent litigation longer than we could. The uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our research and development, in-license needed technology, or enter into strategic partnerships.

Any claims by third parties that we have misappropriated their confidential information or trade secrets could have a similar negative impact on our business. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could significantly harm our business and operating results. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

While inarigivir and SB 11285 are being observed in preclinical studies and/or clinical trials, we believe that the use of inarigivir and SB 11285 in these preclinical studies and/or clinical trials falls within the scope of the exemptions provided by 35 U.S.C. Section 271(e) in the United States, which exempts from patent infringement liability activities reasonably related to the development and submission of information to the FDA. If these product candidates progress toward commercialization, the possibility of a patent infringement claim against us increases. We attempt to ensure that the methods we employ to manufacture inarigivir and SB 11285, as well as the methods for their use that we intend to promote, do not infringe other parties' patents and other proprietary rights. There can be no assurance they do not, however, and competitors or other parties may assert that we infringe their proprietary rights in any event.

In addition, we plan to evaluate inarigivir and SB 11285 in combination with other product candidates and approved products that are covered by patents held by other companies or institutions. In the event that a labeling instruction is required in product packaging recommending that combination, we could be accused of, or held liable for, infringement of the third-party patents covering the product candidate or product recommended for administration with inarigivir or SB 11285. In such a case, we could be required to obtain a license from the other company or institution to use the required or desired package labeling, which may not be available on commercially reasonable terms, or at all.

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

Filing, prosecuting and defending patents on inarigivir, SB 11285, SB 9225 and any other product candidates throughout the world would be prohibitively expensive, and our or our licensors' intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws and practices of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we and our licensors may not be able to prevent third parties from practicing our and our licensors' inventions in all countries outside the United States, or from selling or importing products made using our and our licensors' inventions in or 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 export otherwise infringing products to territories where we or our licensors have patent protection, but where enforcement is not

as strong as in the United States. These products may compete with our products in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our or our licensor's patents or marketing of competing products in violation of our proprietary rights generally in those countries. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business, could put our and our licensors' patents at risk of being invalidated or interpreted narrowly and our and our licensors' patent applications at risk of not issuing and could provoke third parties to assert claims against us or our licensors. We or our licensors may not prevail in any lawsuits that we or our licensors initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful.

The laws of certain foreign countries may not protect our rights to the same extent as the laws of the United States, and these foreign laws may also be subject to change. For example, methods of treatment and manufacturing processes may not be patentable in certain jurisdictions, and the requirements for patentability may differ in certain countries, particularly developing countries. 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. Many countries, including European Union countries, India, Japan and China, have compulsory licensing laws under which a patent owner may be compelled under certain circumstances 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.

A number of foreign countries have stated that they are willing to issue compulsory licenses to patents held by innovator companies on approved drugs to allow the government or one or more third-party companies to sell the approved drug without the permission of the innovator patentee where the foreign government concludes it is in the public interest. India, for example, has used such a procedure to allow domestic companies to make and sell patented drugs without innovator approval. There is no guarantee that patents covering any of our drugs will not be subject to a compulsory license in a foreign country, or that we will have any influence over if or how such a compulsory license is granted. Further, Brazil allows its regulatory agency, ANVISA, to participate in deciding whether to grant a drug patent in Brazil, and patent grant decisions are made based on several factors, including whether the patent meets the requirements for a patent and whether such a patent is deemed in the country's interest. In addition, several other countries have created laws that make it more difficult to enforce drug patents than patents on other kinds of technologies. Further, under the treaty on the Trade-Related Aspects of Intellectual Property, or TRIPS, as interpreted by the Doha Declaration, countries in which drugs are manufactured are required to allow exportation of the drug to a developing country that lacks adequate manufacturing capability. Therefore, our drug markets in the United States or foreign countries may be affected by the influence of current public policy on patent issuance, enforcement or involuntary licensing in the healthcare area.

In November 2015, members of the World Trade Organization, or the WTO, which administers TRIPS, voted to extend the exemption against enforcing pharmaceutical drug patents in least developed countries until 2033. We currently have no patent applications filed in least developed countries, and our current intent is not to file in these countries in the future, at least in part due to this WTO pharmaceutical patent exemption.

The terms of our patents may be inadequate to protect our competitive position on our products for an adequate amount of time.

Given the amount of time required for the development, testing and regulatory review of new product candidates, such as inarigivir, patents protecting such candidates might expire before or shortly after such candidates are commercialized. For instance, certain patents for inarigivir begin to expire in December 2026, without considering any potential patent term adjustments or extensions. We expect to seek extensions of patent terms in the United States and, if available, in other countries where we are prosecuting patents. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years beyond the normal expiration of the patent, which is limited to the approved indication (or any additional indications approved during the period of extension). However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

Changes in patent law, including recent patent reform legislation, could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

As is the case with other biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology and pharmaceutical industries involves technological and legal complexity, and is costly, time-consuming, and inherently uncertain. 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. For example, the United States Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our and our licensors' 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 Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our and our licensors' ability to obtain new patents or to enforce existing patents and patents we and our licensors may obtain in the future. Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our and our licensors' patent applications and the enforcement or defense of our or our licensors' issued patents and those licensed to us.

In September 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the United States transitioned in March 2013 to a "first to file" system in which the first inventor to file a patent application will be entitled to the patent. We may be subject to a third party preissuance submission of prior art to the USPTO or become involved in opposition, derivation, revocation, reexamination, post-grant and *inter partes* review or interference proceedings challenging our patent rights or the patent rights of others. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Furthermore, an adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, 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 medicines without infringing third-party patent rights.

The USPTO continues to develop regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, did not become effective until March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act 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 U.S. Supreme Court has issued opinions in patent cases in the last few years that many consider may weaken patent protection in the United States, either by narrowing the scope of patent protection available in certain circumstances, holding that certain kinds of innovations are not patentable or generally otherwise making it easier to invalidate patents in court. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

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

Periodic maintenance 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, but are not limited to, 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 product candidates, our competitive position would be adversely affected.

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

In addition to patents, we rely on trade secrets, technical know-how and proprietary information concerning our business strategy in order to protect our competitive position with respect to our technology and product candidates. Trade secrets are difficult

to protect, and it is possible that our trade secrets and know-how will over time be disseminated within the industry through independent development and intentional or inadvertent disclosures.

We seek to protect our trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, strategic partners, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and intentionally or inadvertently disclose or use 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 third party illegally obtained and is using any of our trade secrets is expensive and time consuming and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets or the equivalent knowledge, methods and know-how were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be harmed. If we do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

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

Our reliance on third parties to develop and manufacture our product candidates is based upon agreements that limit the rights of the third parties to use or disclose our confidential information, including our trade secrets and know-how. Despite these contractual provisions, the need to share trade secrets and other confidential information increases the risk that such trade secrets and information are disclosed or used, even if unintentionally, in violation of these agreements. In the highly competitive markets in which our product candidates are expected to compete, protecting our trade secrets, including our strategies for addressing competing products, is imperative, and any unauthorized use or disclosure could impair our competitive position and may have a material adverse effect on our business and operations.

In addition, certain of our collaboration partners are larger, more complex organizations than ours, and the risk of inadvertent disclosure of our proprietary information may be increased despite their internal procedures and contractual obligations in place with our collaboration partner. Despite our efforts to protect our trade secrets and other confidential information, a competitor's discovery of such trade secrets and information could impair our competitive position and have an adverse impact on our business.

We may become involved in lawsuits to protect or enforce our intellectual property or in which third parties assert that our licensors, employees or we have misappropriated their intellectual property. We may also be involved in lawsuits in which third parties assert their ownership of intellectual property that we regard as our intellectual property. These lawsuits could be expensive, time consuming and unsuccessful from our perspective and have a material adverse effect on the success of our business.

As is common in the biotechnology and pharmaceutical industries, many of our employees, including our senior management, and our licensors' employees, were previously employed at universities or at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Some of these employees, including each member of our senior management, executed proprietary rights, non-disclosure and non-competition agreements, or similar agreements, in connection with such previous employment. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such third party.

We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property rights. We may also have, in the future, ownership disputes arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates. In addition, competitors or other third parties may infringe our patents or misappropriate or otherwise violate our intellectual property rights.

Litigation may be necessary to enforce or defend our intellectual property rights or to determine the validity and scope of our own intellectual property rights or the proprietary rights of others. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their intellectual property rights, in addition to counterclaims asserting that our intellectual property rights are invalid or unenforceable, or both. Our efforts in any litigation may fail and, even if our efforts in a litigation are successful, may result in substantial costs and require extensive attention from our management and other employees, which could harm our business and financial results.

Despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating our intellectual property, and we may not be able to successfully defend ourselves in similar claims made against us. In any infringement proceeding, a court may decide that intellectual property owned by or licensed to us is invalid or unenforceable or may refuse to stop the other party from using the technology at issue because our intellectual property rights or the intellectual property rights licensed to us do not cover the technology in question.

An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be further harmed if the prevailing party does not offer us a license on commercially reasonable terms. 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 a material adverse effect on the price of shares of our common stock.

Because inarigivir, SB 11285, SB 9225 and any other product candidates we may develop are small molecules, after commercialization they will be subject to the patent litigation process of the Hatch-Waxman Act, which allows a generic company to submit an Abbreviated New Drug Application, or ANDA, to the FDA to obtain approval to sell our drug using bioequivalence data only. Under the Hatch-Waxman Act, since our candidates will be considered new chemical entities, we will have the opportunity to list all of our patents that cover our drug product or its method of use in the FDA's compendium of "Approved Drug Products with Therapeutic Equivalence Evaluation," sometimes referred to as the FDA's Orange Book. A generic company can submit an ANDA to the FDA four years after our drug approval. The submission of the ANDA by a generic company is considered a technical act of patent infringement. The generic company can certify that it will wait until the natural expiration date of our listed patents to sell a generic version of our product or can certify that one or more of our listed patents are invalid, unenforceable, or not infringed. If the latter, we will have 45 days to bring a patent infringement lawsuit against the generic company. This will initiate a challenge to one or more of our Orange Book-listed patents based on arguments from the generic company that either our patent is invalid, unenforceable or not infringed. Under the Hatch-Waxman Act, if a lawsuit is brought, the FDA is prevented from issuing a final approval on the generic drug until the earlier of seven-and-a-half years from our drug approval or a final decision of a court holding that our asserted patent claims are invalid, unenforceable or not infringed. If we do not properly list our relevant patents in the Orange Book, timely file a lawsuit in response to a certification from a generic company under an ANDA or prevail in the resulting patent litigation, we can lose our proprietary market, which can rapidly become generic. Further, even if we do correctly list our relevant patents in the Orange Book, bring a lawsuit in a timely manner and prevail in that lawsuit, it may be at a very significant cost to us of attorneys' fees and employee time and distraction over a long period. Further, it is common for more than one generic company to try to sell an innovator drug at the same time, so we may be faced with the cost and distraction of multiple lawsuits. We may also determine it is necessary to settle the lawsuit in a manner that allows the generic company to enter our market prior to the expiration of our patent or otherwise in a manner that adversely affects the strength, validity or enforceability of our patent.

A number of pharmaceutical companies have been the subject of intense review by the U.S. Federal Trade Commission, or FTC, or a corresponding agency in another country based on how they have conducted or settled drug patent litigation, and certain reviews have led to an allegation of an antitrust violation, sometimes resulting in a fine or loss of rights. We cannot be sure that we would not also be subject to such a review or that the result of the review would be favorable to us, which could result in a fine or penalty.

The FTC has brought a number of lawsuits in federal court in the past few years to challenge Hatch- Waxman ANDA litigation settlements between innovator companies and generic companies as anti-competitive. The FTC has taken an aggressive position that anything of value is a payment, whether money is paid or not. Under their approach, if an innovator as part of a patent settlement agrees not to launch or delay launch of an authorized generic during the 180-day period granted to the first generic company to challenge an Orange Book- listed patent covering an innovator drug, or negotiates a delay in entry without payment, the FTC may consider it an unacceptable reverse payment. The biopharmaceutical industry argues that such agreements are rational business decisions to dismiss risk and are immune from antitrust attack if the terms of the settlement are within the scope of the exclusionary potential of the patent. In 2013, the U.S. Supreme Court, in a five-to-three decision in FTC v. Actavis, Inc., rejected both the biopharmaceutical industry's and FTC's arguments with regard to so-called reverse payments, and held that whether a "reverse payment" settlement involving the exchange of consideration for a delay in entry is subject to an anticompetitive analysis depends on five considerations: (a) the potential for genuine adverse effects on competition; (b) the justification of payment; (c) the patentee's ability to bring about anticompetitive harm; (d) whether the size of the payment is a workable surrogate for the patent's weakness; and (e) that antitrust liability for large unjustified payments does not prevent litigating parties from settling their lawsuits, for example, by allowing the generic to enter the market before the patent expires without the patentee's paying the generic. Furthermore, whether a reverse payment is justified depends upon its size, its scale in relation to the patentee's anticipated future litigation costs, its independence from other services for which it might represent payment, as was the case in Actavis, and the lack of any other convincing justification. The Court held that reverse payment settlements can potentially violate antitrust laws and are subject to the standard antitrust rule-of-reason analysis, with the burden of proving that an agreement is unlawful on the FTC and leaving to lower courts the structuring of such rule of reason analysis. If we are faced with drug patent litigation, including Hatch-Waxman litigation

with a generic company, we could be faced with such an FTC challenge based on that activity, including how or whether we settle the case, and even if we strongly disagree with the FTC's position, we could face a significant expense or penalty.

Risks Related to Employee Matters and Managing Growth

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

As of February 28, 2019, we had 29 full-time employees, 16 of whom hold Ph.D. or M.D. degrees. As our development and commercialization plans and strategies develop, we will need additional managerial, operational, sales, marketing, financial and other resources. Our management, personnel and systems currently in place are likely not adequate to support this future growth. Future growth would impose significant added responsibilities on members of management, including:

- managing our clinical trials effectively;
- identifying, recruiting, maintaining, motivating and integrating additional employees;
- managing our internal development efforts effectively while complying with our contractual obligations to licensors, licensees, contractors and other third parties;
- improving our managerial, development, operational and finance systems; and
- expanding our facilities.

Our management may need to devote a disproportionate amount of its attention to managing these growth activities. 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 identify, recruit and train additional qualified personnel. Our inability to manage the expansion of our operations effectively may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could also require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If we are unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate revenues could be reduced and we may not be able to implement our business strategy, including the successful commercialization of our product candidates.

Our future success depends on our ability to retain our executive officers and to attract, retain and motivate qualified personnel.

We are highly dependent upon Martin Driscoll, our president and chief executive officer; Nezam Afdhal, MD, our chief medical officer; and Radhakrishnan P. Iyer, Ph.D., our chief scientific officer. We have entered into employment agreements with each of these executive officers. These employment agreements do not prevent such persons from terminating their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

Our ability to compete in the highly competitive biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. Our industry has experienced a high rate of turnover of management personnel in recent years. If we lose one or more of our executive officers or other key employees, our ability to implement our business strategy successfully could be seriously harmed. Furthermore, replacing executive officers or other key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain marketing approval of and commercialize products successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key employees on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions.

We rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by other entities and may have commitments under consulting or advisory contracts with those entities that may limit their availability to us. If we are unable to continue to attract and retain highly qualified personnel, our ability to develop and commercialize our product candidates will be limited.

Risks Related to Our Common Stock

The trading market in our common stock has been limited and substantially less liquid than the average trading market for a stock quoted on The Nasdaq Capital Market.

Since our initial listing on The Nasdaq Capital Market on May 6, 2016, the trading market in our common stock has been extremely limited and substantially less liquid than the average trading market for companies quoted on The Nasdaq Capital Market. The quotation of our common stock on The Nasdaq Capital Market does not assure that a meaningful, consistent and liquid trading market currently exists. We cannot predict whether a more active market for our common stock will develop in the future. An absence of an active trading market could adversely affect your ability to sell our common stock at current market prices in short time periods, or possibly at all. Additionally, sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock even if our business is doing well. Ultimately, market visibility for our common stock may be limited and such lack of visibility may have a depressive effect on the market price for our common stock.

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for our stockholders.

Our stock price is likely to be volatile. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. Because of this volatility, you may not be able to sell your common stock at or above the price at which you purchased your shares. The market price for our common stock may be influenced by many factors, including:

- results of clinical trials of our product candidates or those of our competitors;
- the success of competitive products or technologies;
- developments related to any future collaborations;
- regulatory or legal developments in the United States and other countries;
- development of new product candidates that may address our markets and may make our product candidates less attractive;
- changes in physician, hospital or healthcare provider practices that may make our product candidates less useful;
- announcements by us, our partners or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

Our executive officers and directors and their affiliates, if they choose to act together, may have the ability to significantly influence all matters submitted to stockholders for approval.

As of December 31, 2018, our executive officers and directors and their affiliates beneficially owned shares representing approximately 12% of our outstanding common stock, and this group, together with other stockholders holding beneficially 5% of more of our outstanding common stock, owned approximately 40% of our outstanding common stock. If these stockholders were to choose to act together, they may be able to significantly influence matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, may be able to significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of ownership control may:

- delay, defer or prevent a change in control;
- entrench our management and the board of directors; or
- impede a merger, consolidation, takeover or other business combination involving us that other stockholders may desire.

We are an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an emerging growth company, as defined in the JOBS Act, and may remain an emerging growth company until the last day of the fiscal year following the fifth anniversary of the closing of our initial public 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. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- being permitted to provide 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;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; 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 have taken advantage of these reduced reporting burdens. In particular, in connection with our recent offerings, we have provided only two years of audited financial statements and we have not included all of the executive compensation related information that would be required if we were not an emerging growth company. We expect to continue to take advantage of some or all of the reporting exemptions available to emerging growth companies. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be reduced or more volatile. In addition, 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. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

We incur increased costs as a result of operating as a public company and our management is required to devote substantial time to compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an emerging growth company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the exchange or market upon which we trade and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased 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 officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors.

We cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. 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 regulatory and governing bodies provide new guidance. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we are not required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting.

If we fail to maintain an effective system of disclosure controls and internal control over financial reporting, our ability to produce timely and accurate financial statements or comply with applicable regulations could be impaired.

As a public company, we are subject to the reporting requirements of the Securities and Exchange Commission, the Sarbanes-Oxley Act and the listing standards of The Nasdaq Stock Market, the exchange on which our common stock is listed. We expect that the requirements of these rules and regulations will continue to increase our legal, accounting and financial compliance costs, make some activities more difficult, time consuming and costly and place significant strain on our personnel, systems and resources.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. We are continuing to refine our disclosure controls and other procedures that are designed to ensure that the information that we are required to disclose in the reports that we will file with the Securities and Exchange Commission is properly recorded, processed, summarized and reported within the time periods specified in SEC rules and forms. We are also continuing to improve our internal control over financial reporting. We have expended, and anticipate that we will continue to expend, significant resources in order to maintain and improve the effectiveness of our disclosure controls and procedures and internal control over financial reporting.

Our current controls and any new controls that we develop in the future may become inadequate because of changes in conditions in our business. Further, weaknesses in our disclosure controls or our internal control over financial reporting may be discovered in the future. Any failure to develop or maintain effective controls, or any difficulties encountered in their implementation or improvement, could harm our operating results or cause us to fail to meet our reporting obligations and may result in a restatement of our financial statements for prior periods. Any failure to implement and maintain effective internal control over financial reporting could also adversely affect the results of management reports and independent registered public accounting firm audits of our internal control over financial reporting that we will be required to include in our periodic reports that will be filed with the Securities and Exchange Commission. If we were to have ineffective disclosure controls and procedures or internal control over financial reporting, our investors could lose confidence in our reported financial and other information, which would likely have a negative effect on the market price of our common stock.

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline.

The trading market for our common stock may be influenced by the research and reports that industry or securities analysts publish about us or our business. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our preclinical studies or clinical trials and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Provisions in our restated certificate of incorporation and amended and restated bylaws and under Delaware law could make an acquisition of our Company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our restated certificate of incorporation and our amended and restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our Company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. 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 stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions include those establishing:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from filling vacancies on our board of directors;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer;
- the ability of our board of directors to alter our bylaws without obtaining stockholder approval;
- the required approval of the holders of at least a majority of the shares entitled to vote at an election of directors to adopt, amend or repeal our bylaws or repeal the provisions of our restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by the board of directors, the chairman of the board of directors, the chief executive officer or stockholders holding a majority of our issued and outstanding common stock, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of us.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. Furthermore, our amended and restated bylaws specify that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for most legal actions involving actions brought against us by stockholders. We believe this provision benefits us by providing increased consistency in the application of Delaware law by chancellors particularly experienced in resolving corporate disputes, efficient administration of cases on a more expedited schedule relative to other forums

and protection against the burdens of multi-forum litigation. However, the provision may have the effect of discouraging lawsuits against our directors and officers. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any applicable action brought against us, a court could find the choice of forum provisions contained in our restated certificate of incorporation to be inapplicable or unenforceable in such action.

Our ability to use our net operating loss and credit carryforwards to offset future taxable income may be subject to certain limitations.

At December 31, 2018, we had potentially utilizable federal and state net operating loss carryforwards of approximately $86.3 million and $86.4 million, respectively. The federal net operating loss carryforwards of $61.5 million expire between 2029 and 2037 and $24.8 million carryforward indefinitely. The state net operating loss carryforwards expire between 2030 and 2038. Our ability to utilize our net operating loss and credit carryforwards is dependent upon our ability to generate taxable income in future periods and may be limited due to restrictions imposed on utilization of net operating loss and credit carryforwards under federal and state laws upon a change in ownership.

Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Internal Revenue Code, a corporation that undergoes an "ownership change," is subject to limitations on its ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change income or taxes. For these purposes, an ownership change generally occurs where the equity ownership of one or more stockholders or groups of stockholders who owns at least 5% of a corporation's stock increases its ownership by more than 50 percentage points over its lowest ownership percentage within a three-year period (calculated on a rolling basis). We have made a preliminary determination that an ownership change likely occurred in each of April 2012 and December 2013. However, we anticipate that all of our approximately $86.3 million and $86.4 million of federal and state NOLs, respectively, will be available to us to offset future taxable income. We may have experienced other ownership changes in the past, and we may experience ownership changes in the future, some of which are outside the Company's control. These ownership changes may subject our existing net operating losses or credits to substantial limitations under Sections 382 and 383. Accordingly, we may not be able to utilize a material portion of our net operating losses or credits. Limitations on our ability to utilize our net operating losses to offset U.S. federal taxable income could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of net operating losses is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

Because U.S. federal net operating losses arising in taxable years beginning before January 1, 2018 generally may be carried forward for up to 20 years, the annual limitation may effectively provide a cap on the cumulative amount of pre-ownership change losses, including certain recognized built-in losses that may be utilized. Such pre-ownership change losses in excess of the cap may be lost. In addition, if an ownership change were to occur, it is possible that the limitations imposed on our ability to use pre-ownership change losses and certain recognized built-in losses could cause a net increase in our U.S. federal income tax liability and require U.S. federal income taxes to be paid earlier than otherwise would be paid if such limitations were not in effect. Further, if for financial reporting purposes the amount or value of these deferred tax assets is reduced, such reduction would have a negative impact on the book value of our common stock.

Net operating losses, if any, arising in taxable years beginning after December 31, 2017 may be subject to limitation under Sections 382 and 383 of the Internal Revenue Code as discussed above, but will be subject to the further limitation, adopted by the JOBS Act, that in any year such NOL may offset no more than 80 percent of such year's taxable income (computed without regard to any deduction for net operating loss carryover). As a result of limiting the deduction for post-2017 NOLs to no more than 80% of current year taxable income, we may be required to pay federal income tax in some future year notwithstanding that we have a net loss for all years in the aggregate.

Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

We have never declared or paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

We could be subject to securities class action litigation.

When the market price of a stock is volatile, holders of that stock have often initiated securities class action litigation against the company that issued the stock. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business. We may not be successful in defending ourselves or asserting our rights in future lawsuits, investigations, or claims that may be brought against us and, as a result, our business could be materially

harmed. These lawsuits, arbitrations, investigations or claims may result in large judgments or settlements against us, any of which could have a negative effect on our financial performance and business. Additionally, lawsuits, arbitrations and investigations can be expensive to defend, whether or not the lawsuit, arbitration or investigation has merit, and the defense of these actions may divert the attention of our management and other resources that would otherwise be engaged in running our business

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 2. Properties.

Our current operations are based in Hopkinton, Massachusetts. A description of the facilities we lease as of December 31, 2018 is included in the table below.

Location	Primary Use	Approximate Square Footage	Lease Expiration Date	Renewal Option
35 Parkwood Drive Hopkinton, Massachusetts	Corporate headquarters	31,315	October 2028	One five-year term
86 South Street Hopkinton, Massachusetts	Former corporate headquarters[(1)]	12,200	May 2021	One five-year term

(1) – Property subject to sublease agreement.

Item 3. Legal Proceedings.

From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. We are not presently a party to any material litigation.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Our common stock began trading on The Nasdaq Capital Market on May 6, 2016 under the symbol "SBPH". Prior to that time, there was no established public trading market for our common stock. On March 6, 2019, the closing price of our common stock was $10.15 per share.

Holders of Record

As of March 6, 2019, we had 16,436,895 outstanding shares of common stock and no outstanding shares of preferred stock. At March 6, 2019, there were 81 holders of record of our common stock. Because many of our shares are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of beneficial holders represented by these record holders.

Sales of Unregistered Securities

Not applicable.

Issuer Purchases of Equity Securities

Not applicable.

Item 6. Selected Financial Data.

The following selected consolidated financial data should be read together with our consolidated financial statements and accompanying notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations" appended to this Annual Report on Form 10-K. The selected consolidated financial data in this section are not intended to replace our consolidated financial statements and the related notes. Our historical results are not necessarily indicative of the results that may be expected in the future.

The selected consolidated statement of operations and consolidated balance sheet data for the years ended December 31, 2018 and 2017 are derived from our audited consolidated financial statements appended to this Annual Report on Form 10-K (in thousands, except share and per share data).

	Year Ended December 31,	
	2018	2017
Consolidated Statement of Operations Data:		
Operating expenses:		
Research and development	$ 19,751	$ 13,075
General and administrative	8,719	8,178
Total operating expenses	28,470	21,253
Loss from operations	(28,470)	(21,253)
Interest income, net	999	369
Change in fair value of warrant liabilities	4,617	(6,795)
Net loss	$ (22,854)	$ (27,679)
Net loss per common share:		
Basic	$ (1.59)	$ (2.48)
Diluted	$ (1.88)	$ (2.48)
Weighted-average number of shares outstanding:		
Basic	14,372,174	11,153,269
Diluted	14,618,976	11,153,269

(1) See Notes 1 and 2 to our consolidated financial statements appended to this Annual Report on Form 10-K for further details on the calculation of basic and diluted net loss per common share.

	As of December 31,	
	2018	2017
Consolidated Balance Sheet Data:		
Cash, cash equivalents and marketable securities	$ 64,442	$ 50,555
Working capital	45,040	46,701
Total assets	68,811	52,341
Total stockholders' equity	55,860	34,748

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

You should read the following discussion and analysis of financial condition and results of operations together with Item 6 of this Annual Report on Form 10-K titled "Selected Financial Data" and our consolidated financial statements and related notes appended to this Annual Report on Form 10-K. This discussion and other parts of this Annual Report on Form 10-K contain forward-looking statements that involve risks and uncertainties, such as statements regarding our plans, objectives, expectations, intentions and projections. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in Item 1A, "Risk Factors" of this Annual Report on Form 10-K.

Overview

We are a clinical-stage biopharmaceutical company engaged in the discovery and development of a novel class of therapeutics for the treatment of viral infections, inflammatory diseases and certain cancers using our proprietary small molecule nucleotide platform. We design our compounds to selectively target and modulate the activity of specific proteins implicated in various disease states. We are developing our lead product candidate, inarigivir, for the treatment of HBV. We have designed our antiviral product candidates, including inarigivir, to selectively activate within infected hepatic cells the cellular protein, RIG-I, to inhibit viral replication and to cause the induction of intracellular interferon signaling pathways for antiviral defense. We believe that inarigivir, as a RIG-I agonist, could play an important role in antiviral therapy as a result of its dual mechanism of action that is designed to selectively modulate the body's immune response and inhibit viral replication. We are also developing additional product candidates, including our lead STING agonist product candidate, SB 11285, which is an immunotherapeutic agent for the potential treatment of selected cancers.

Inarigivir Clinical Trial Strategy. We are developing our lead product candidate, inarigivir, an orally-administered hepatic-selective immunomodulator, as a potential backbone in a combinatorial treatment for chronic HBV with the goal to accelerate and substantially increase chronic HBV functional cure rates in a simple, safe and selective manner.

ACHIEVE Trial. We are currently evaluating inarigivir for the treatment of chronic HBV in a global Phase 2 multi-center clinical trial of inarigivir, which we refer to as the ACHIEVE trial. The ACHIEVE trial is being conducted under our first clinical trial supply and collaboration with Gilead. Approximately 80 treatment-naive patients infected with chronic HBV have received doses of 25mg, 50mg, 100mg or 200mg of inarigivir or a placebo as a monotherapy administered daily for 12 weeks, followed by all patients receiving a sequential dose of Viread® for 12 weeks. The active-placebo randomization schedule was 4:1 in the inarigivir monotherapy dosing period.

In the first three cohorts (25mg, 50mg and 100mg) of the ACHIEVE trial, 13 of 47 patients (28%) had a 0.5 $\log_{10}$ or greater reduction in HBsAg. Of these 13 responder patients, six were HBeAg-negative (-) patients and seven were HBeAg-positive (+) patients. Additionally, we have observed a dose dependent response of inarigivir on HBV DNA and HBV RNA over the first three cohorts. To date, inarigivir has been well tolerated in the ACHIEVE trial, with no inarigivir-related serious adverse events observed, and no flu-like symptoms or other interferon-like side effects.

All patients in the final 200mg cohort of the ACHIEVE trial have completed dosing of Viread.

Gilead Collaboration. In July 2017, we entered into our second clinical trial collaboration agreement with Gilead under which Gilead is funding and conducting a Phase 2 clinical trial examining the co-administration of inarigivir and Vemlidy in patients infected with chronic HBV. This clinical trial collaboration was expanded in August 2018 to include two additional cohorts. In the first cohort of this Phase 2 trial, treatment-naive patients received 12 weeks of combination therapy with inarigivir 50mg and Vemlidy, while in the second cohort treatment-naive patients are receiving 12 weeks of combination therapy with inarigivir 200mg and Vemlidy. In a third cohort, Gilead is evaluating the administration of inarigivir 100mg in virally-suppressed patients who are already are and continue to be treated with a NUC. While we have approved the protocol for this trial under a joint steering committee, Gilead is conducting this trial at their own expense.

CATALYST Trials. We plan to initiate in the first half of 2019 two major Phase 2 global trials examining the administration of inarigivir 400mg in different patient populations and under different dosing regimens. We anticipate that the first global trial will be conducted in Asia and the U.S. and will evaluate non-cirrhotic, treatment-naïve HBeAg positive and negative patients infected with chronic HBV who receive inarigivir 400mg as both(i) monotherapy for 12 weeks followed by the sequential treatment of Vemlidy for 12 weeks, and (ii) in combination with Vemlidy for 24 weeks. We refer to this trial as the CATALYST 1 trial. Pre-defined responder patients at week 24 will continue to receive inarigivir 400mg and Vemlidy for up to an additional 24 weeks to determine if they are able to achieve a functional cure.

Concurrent with the CATALYST 1 trial, we plan to initiate a separate trial, which we refer to as the CATALYST 2 trial, in the United Kingdom and Canada examining the use of inarigivir 400mg in non-cirrhotic, virally-suppressed patients currently on a NUC (i) following the cessation of treatment with a NUC, which we refer to as "Stop and Shock" treatment, and (ii) with the continued dosing of a NUC, which we refer to as "Suppress and Shock" treatment. Under the "Stop and Shock" treatment, patients will receive inarigivir 400mg for 24 weeks and then stop all treatment to evaluate for loss of HBsAg or sustained viral suppression over time, up to 18 months. Under the "Suppress and Shock" treatment, patients will receive inarigivir 400mg, in addition to their current NUC treatment, for a period of 24-48 weeks, and again stop all treatment with a follow up to see if there is either loss of HBsAg or sustained viral suppression off treatment. Pending preliminary results from the CATALYST studies, we plan to conduct a separate "Suppress and Shock" trial in the United States and the European Union, potentially in the second half of 2019. This trial could evaluate the efficacy of inarigivir 400mg over the course of 48 weeks in virally-suppressed patients when compared to the use of a NUC alone.

Fixed-Dose Combination (SB 9225). We are also pursuing the development of SB 9225, a co-formulation of inarigivir with tenofovir disoproxil fumarate, as a potential fixed-dose combination product for the treatment of patients with chronic HBV. We have conducted early development work that indicates compatibility of inarigivir with Viread in the same formulation. We have conducted additional formulation development work for SB 9225 and successfully manufactured initial quantities of SB 9225. The introduction of SB 9225, if approved, could potentially result in enhanced patient compliance and allow for a more favorable safety profile. Subject to the results of our Phase 2 inarigivir trials, we could be in a position to initiate a Phase 3 program for SB 9225 in the United States, Europe and Asia in 2020.

Immuno-Oncology Program. We are developing our lead STING agonist product candidate, SB 11285, as a second-generation immunotherapeutic agent for the treatment of selected cancers. In our preclinical studies in multiple tumor-derived cell lines, SB 11285 has been observed to cause the induction of cytokines consistent with engagement of the STING target, as well as cell death and apoptosis. Based on our preclinical studies performed to date, SB 11285 has reduced tumor volumes in multiple rodent tumor models when administered intravenously or intratumorally. These findings lead us to believe that SB 11285 has the potential to be administered clinically by either route of administration, and that SB 11285 may be used to target a variety of tumors at various anatomic sites and, if approved, has the potential to be used in combination with other therapeutic modalities to enhance efficacy.

We are currently advancing the SB 11285 program with preclinical, toxicology, and process development efforts. Subject to the results of these preclinical studies, we anticipate that we will submit an IND for SB 11285 in the second quarter of 2019, and, if approved, initiate a Phase 1/2 clinical trial in cancer later in 2019. SB 11285 could be the first intravenously-administered STING agonist product candidate to enter clinical development.

Financial Operations Overview

To date, we have devoted substantially all of our resources to research and development efforts, including conducting preclinical studies and clinical trials for our product candidates, protecting our intellectual property and providing general and administrative support for these operations. We have not generated any revenue to date other than from grants from the National Institutes of Health, or NIH. We have incurred significant annual net operating losses in every year since our inception and expect to continue to incur significant expenses and net operating losses for the next several years. Our net losses were $22.9 million and $27.7 million for the years ended December 31, 2018 and 2017, respectively. As of December 31, 2018, we had an accumulated deficit of $102.1 million. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase significantly as we continue to develop inarigivir, SB 11285, SB 9225 and our other product candidates. See "—Liquidity and Capital Resources—Funding Requirements." As a result, we will need additional financing to support our continuing operations. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of public or private equity or debt financings, including our at-the-market offering program with Cantor Fitzgerald & Co., or other sources, which may include collaborations with third parties. Arrangements with collaborators or others may require us to relinquish rights to certain of our technologies or product candidates. Adequate additional financing may not be available to us on acceptable terms, or at all. Our inability to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. We will need to generate significant revenue to achieve and sustain profitability, and we may never be able to do so.

As of December 31, 2018, we had $64.4 million in cash, cash equivalents and marketable securities. We expect that our cash, cash equivalents and marketable securities as of December 31, 2018 will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2021. We have based this estimate on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. See "—Liquidity and Capital Resources."

Operating expenses

Our operating expenses since inception have consisted primarily of research and development expense and general and administrative costs.

Research and development

Research and development expenses consist primarily of costs incurred for our research activities, including our discovery efforts, and the development of our product candidates, which include:

- expenses incurred under agreements with third parties, including contract research organizations, or CROs, that conduct research, preclinical activities and clinical trials on our behalf as well as contract manufacturing organizations, or CMOs, that manufacture drug products for use in our preclinical and clinical trials;
- salaries, benefits and other related costs, including stock-based compensation expense, for personnel in our research and development functions;
- costs of outside consultants, including their fees, stock-based compensation and related travel expenses;
- the cost of laboratory supplies and acquiring, developing and manufacturing preclinical study and clinical trial materials;
- costs related to compliance with regulatory requirements; and
- facility-related expenses, which include direct depreciation costs and allocated expenses for rent, maintenance of facilities, equipment, insurance and other operating costs.

We expense research and development costs as incurred. We recognize external development costs based on an evaluation of the progress to completion of specific tasks using information provided to us by our vendors and our clinical investigative sites. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our consolidated financial statements as prepaid or accrued research and development expenses.

Our direct research and development expenses are not currently tracked on a program-by-program basis. Our primary focus has been on the research and development of inarigivir. Our direct research and development expenses consist primarily of external costs, such as fees paid to investigators, consultants and CROs in connection with our preclinical studies and clinical trial and regulatory fees. We do not allocate employee-related costs and other indirect costs to specific research and development programs because our primary focus has been on the research and development of inarigivir.

The successful development of our product candidates is highly uncertain. Accordingly, at this time, we cannot reasonably estimate the nature, timing and costs of the efforts that will be necessary to complete the development of any of our product candidates. We are also unable to predict when, if ever, we will generate revenues from inarigivir or any of our other product candidates. This is due to the numerous risks and uncertainties associated with developing medicines, including the uncertainties of:

- establishing an appropriate safety profile with investigational new drug, or IND, application enabling toxicology studies;
- successful enrollment in and completion of clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- launching commercial sales of the products, if and when approved, whether alone or in collaboration with others; and
- if a product is approved, a continued acceptable safety profile of the product.

A change in the outcome of any of these variables with respect to any of our product candidates would significantly change the costs and timing associated with the development of that product candidate.

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. We expect that our research and development expenses will continue to increase in the foreseeable future as we initiate clinical trials for certain product candidates and pursue later stages of clinical development of other product candidates. However, we do not believe that it is possible at this time to accurately project total program-specific expenses through commercialization. There are numerous factors associated with the successful commercialization of any of our product candidates, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. Additionally, future commercial and regulatory factors beyond our control will impact our clinical development programs and plans.

General and administrative

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in our executive, finance, corporate and business development and administrative functions. General and administrative expenses also include legal fees relating to patent and corporate matters; professional fees for accounting, auditing, tax and consulting services; insurance costs; travel expenses; and facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support the expected growth in our research and development activities and the potential commercialization of our product candidates. We also expect to incur increased expenses associated with being a public company, including increased costs of accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance premiums, and investor and public relations costs.

Other income (expense)

Other income (expense) consists of interest income earned on our cash, cash equivalents, restricted cash and marketable securities.

Change in fair value of warrant liabilities

Change in fair value of warrant liabilities consists of a gain or (loss) related to the change in the fair value of the warrants issued in connection with our private placement offering in November 2016, resulting from a change factors such as a change in our stock price and a change in expected stock price volatility.

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 of America. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and assumptions that affect the reported amount of assets, liabilities, revenue, costs and expenses and related disclosures. We believe that the estimates and assumptions involved in the accounting policies described therein may have the greatest potential impact on our consolidated financial statements and, therefore, consider these to be our critical accounting policies. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions and conditions.

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 costs incurred for the services when we have not yet been invoiced or otherwise notified of the actual costs. The majority of our service providers invoice us in arrears for services performed, on a predetermined 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 our consolidated

financial statements based on facts and circumstances known to us at that time. Examples of estimated accrued research and development expenses include fees paid to:

- CROs in connection with performing research services on our behalf and clinical trials;
- investigative sites or other providers in connection with clinical trials;
- vendors in connection with preclinical and clinical development activities; and
- vendors related to product manufacturing, development and distribution of preclinical and clinical supplies.

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 CROs that conduct and manage 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 clinical 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, enrollment of patients, number of sites activated and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or amount of prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low in any particular period. To date, we have not made any material adjustments to our prior estimates of accrued research and development expenses.

Warrants Issued in 2016 Private Placement

In connection with our private placement offering in November 2016, or the November private placement, we issued warrants to purchase 1,644,737 shares of common stock, which we refer to as the November 2016 Warrants. These warrants are exercisable at an exercise price of $10.79 per share. We evaluated the terms of these warrants and concluded that they should be liability-classified. In November 2016, we recorded the fair value of these warrants of approximately $8.3 million. We recognize any change in the value of the warrant liability each reporting period in the statement of operations. As of December 31, 2018, the fair value of these warrants was approximately $8.5 million, which is a decrease of $4.6 million from the fair value of approximately $13.1 million as of December 31, 2017.

Stock-Based Compensation

We issue stock-based awards to employees and non-employees, generally in the form of stock options. We account for our stock-based compensation awards in accordance with Financial Accounting Standards Board, (FASB) ASC Topic 718, *Compensation—Stock Compensation*, or ASC 718. ASC 718 requires all stock-based payments to employees, including grants of employee stock options and modifications to existing stock awards, to be recognized in the statements of operations and comprehensive loss based on their fair values. We adopted ASU 2018-07, *Improvements to Nonemployee Share-Based Payment Accounting*, effective July 1, 2018, which aligns the accounting treatment of nonemployee awards with employee awards. Described below is the methodology we have utilized in measuring stock-based compensation expense. Stock option, common stock and restricted stock values are determined based on a blend of our stock price and the quoted market price of our comparable public companies.

We measure stock options and other stock-based awards granted to employees, nonemployees and directors based on the fair value on the date of 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. Generally, we issue stock options and restricted stock awards with service-based vesting conditions and record the expense for these awards using the straight-line method. We adopted ASU No. 2016-09, *Compensation-Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting,* or ASU 2016-09, effective January 1, 2017. Prior to adoption, share-based compensation expense was recognized on a straight-line basis, net of estimated forfeitures, such that expense was recognized only for share-based awards that are expected to vest. A forfeiture rate was estimated annually and revised, if necessary, in subsequent periods if actual forfeitures differed from initial estimates. Following adoption of ASU 2016-09, we no longer apply a forfeiture rate and instead will account for forfeitures as they occur.

We estimate the fair value of each stock option grant using the Black-Scholes option-pricing model. Use of this model requires that we make assumptions as to the fair value of our common stock, the volatility of our common stock, 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. Because we lack company-specific historical and implied volatility information due in part to the limited time in which we have operated as a publicly traded company, we estimate our expected volatility based on the historical volatility of a group of publicly traded peer companies. We expect to continue to do so until such time as we have adequate historical data regarding the volatility of our traded stock price. We use the simplified method prescribed by Securities and Exchange Commission Staff Accounting Bulletin No. 107, *Share-Based Payment*, to calculate the expected term of options granted to employees and directors. We base the expected term of options granted to consultants and nonemployees on the contractual term of the options. We determine the risk-free interest rate by reference to the United States 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 we have never paid cash dividends and do not expect to pay any cash dividends in the foreseeable future.

There were no stock options granted prior to 2015. We recognize forfeitures as they occur and the compensation expense for unvested awards is reversed in the period that the forfeiture occurs. The assumptions we used to determine the fair value of granted stock options in 2018 and 2017 are as follows:

	Year Ended December 31,	
	2018	2017
Risk-free interest rate	2.5%	2.0%
Expected term (in years)	5.9	6.0
Expected volatility	82.5%	80%
Expected dividend yield	0%	0%

These assumptions represented our best estimates, but the estimates involve inherent uncertainties and the application of our judgment. As a result, if factors change and we use significantly different assumptions or estimates, our stock-based compensation expense could be materially different. We recognize compensation expense for only the portion of awards that are expected to vest.

During the years ended December 31, 2018 and 2017, we issued common stock to directors as compensation for services and recognized expense equal to the fair value of the shares issued. The following table summarizes the classification of our stock-based compensation expenses recognized in our consolidated statements of operations and comprehensive loss (in thousands):

	Year Ended December 31,	
	2018	2017
Research and development	$ 843	$ 489
General and administrative	1,933	1,422
	$ 2,776	$ 1,911

JOBS Act

In April 2012, the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, was enacted. Section 107 of the JOBS Act provides that an "emerging growth company," or EGC, can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. Thus, an EGC can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

As an EGC, we are relying on certain JOBS Act exemptions, including the exemption from the requirement that the auditors provide an attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and complying with any requirement that may be adopted by the Public Company Accounting Oversight Board, or PCAOB, regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis. We will remain an EGC until the earliest of the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more; the last day of the fiscal year following the fifth anniversary of the date of the completion of the closing of our initial public offering; the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission.

Results of Operations

Comparison of Years Ended December 31, 2018 and 2017

The following table summarizes our results of operations for the years ended December 31, 2018 and 2017 (in thousands):

	Year Ended December 31, 2018	2017	Increase (Decrease)
Operating expenses:			
Research and development	$ 19,751	$ 13,075	$ 6,676
General and administrative	8,719	8,178	541
Total operating expenses	28,470	21,253	7,217
Loss from operations	(28,470)	(21,253)	(7,217)
Other income	999	369	630
Change in fair value of warrant liabilities	4,617	(6,795)	11,412
Net loss	$ (22,854)	$ (27,679)	$ 4,825

Research and development expenses. Research and development expenses were $19.8 million for the year ended December 31, 2018, compared to $13.1 million for the year ended December 31, 2017. The increase of $6.7 million was due primarily to an increase in preclinical studies and clinical trial-related activities for inarigivir and preclinical studies for SB 11285 of $5.1 million, salaries and benefits of $0.6 million associated with higher headcount in the year ended December 31, 2018, non-cash charges for stock-based compensation of $0.4 million, laboratory supplies of $0.2 million, lease and building maintenance costs related costs of $0.2 million, consulting services of $0.1 million and non-cash charges for depreciation of $0.1 million.

General and administrative expenses. General and administrative expenses were $8.7 million for the year ended December 31, 2018, compared to $8.2 million for the year ended December 31, 2017. This increase of $0.5 million was primarily due to an increase in non-cash charges for stock-based compensation of $0.5 million, lease related costs of $0.3 million, loss on disposal of property and equipment of $0.1 million, all of which were offset by a decrease in other general and administrative costs including professional fees, investor relations costs, Delaware Franchise taxes and legal costs of $0.3 million and salaries and benefits of $0.1 million.

Other income. Other income for the years ended December 31, 2018 and 2017 is solely comprised of interest income. Interest income for the years ended December 31, 2018 and 2017 was $1.0 million and $0.4 million, respectively, and was primarily related to the interest earned on marketable securities. The increase in interest income in the year ended December 31, 2018 was due to a higher average balance of marketable securities.

Change in fair value of warrant liabilities. Change in fair value of warrant liabilities for the year ended December 31, 2018 and 2017 was a gain of $4.6 million and a loss of $6.8 million, respectively. The change in value each year was solely related to the change in the fair value of the warrants from the November 2016 Warrants, primarily as a result of the change in the Company's stock price.

Liquidity and Capital Resources

Sources of Liquidity

From our inception through December 31, 2018, we financed our operations through proceeds received from private placements of convertible notes, common stock and/or warrants; the exercise of options and warrants; NIH grant funding; and public offerings. As of December 31, 2018, we had cash, cash equivalents and marketable securities totaling $64.4 million and an accumulated deficit of $102.1 million.

In August 2018, we issued and sold in an underwritten public offering an aggregate of 3,246,079 shares of our common stock at $12.50 per share, which included 246,079 shares pursuant to the exercise of an option to purchase additional shares granted to the underwriters in connection with the offering. The shares issued in this offering were registered under the Securities Act pursuant to our Registration Statement on Form S-3 (Registration No. 333-218399) that was declared effective by the SEC on June 12, 2017, which we refer to as the S-3 Registration Statement, and a prospectus supplement and base prospectus filed on August 9, 2018. The offering resulted in $38.0 million of net proceeds, after deducting underwriting discounts and commissions and other offering expenses payable by us.

In August 2017, we entered into a Controlled Equity Offering℠ Sales Agreement, or Sales Agreement, with Cantor Fitzgerald & Co., or Cantor, pursuant to which we may offer and sell, from time to time through Cantor, shares of our common stock having an aggregate offering price of up to $50.0 million. We will pay Cantor a commission rate equal to 3.0% of the aggregate gross

proceeds from each sale. Shares sold under the Sales Agreement will be offered and sold pursuant to our S-3 Registration Statement , and a prospectus supplement and accompanying base prospectus that we filed with the Securities and Exchange Commission on August 18, 2017. During the year ended December 31, 2018, we sold an aggregate of 217,329 shares of our common stock under the Sales Agreement at a weighted average selling price of $15.42 per share, which resulted in $3.2 million of net proceeds. During the year ended December 31, 2017, we sold an aggregate of 252,443 shares of our common stock pursuant to the Sales Agreement at a weighted-average selling price of $15.55 per share, which resulted in $3.7 million of net proceeds.

In June 2017, we issued and sold in an underwritten public offering an aggregate of 3,269,219 shares of our common stock at $13.00 per share, which included 384,604 shares pursuant to the exercise of an option to purchase additional shares granted to the underwriters in connection with the offering. The shares issued in this offering were registered under the Securities Act pursuant to the S-3 Registration Statement. The offering resulted in $39.7 million of net proceeds, after deducting underwriting discounts and commissions and other offering expenses payable by us.

Cash Flows

The following table summarizes sources and uses of cash for each of the periods presented (in thousands):

	For the Year Ended December 31,	
	2018	2017
Net cash used in operating activities	$ (25,244)	$ (17,683)
Net cash used in investing activities	(25,103)	(12,406)
Net cash provided by financing activities	41,172	43,538
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (9,175)	$ 13,449

Net cash used in operating activities. The use of cash in both periods resulted primarily from our net losses adjusted for non-cash charges and changes in components of working capital. Net cash used in operating activities was $25.2 million and $17.7 million during the years ended December 31, 2018 and 2017, respectively. The increase of $7.5 million in cash used in operating activities during the year ended December 31, 2018 as compared to the year ended December 31, 2017 was primarily due to an increase in prepaid expenses and other current assets and other assets of $1.3 million and an increase in other assets of $0.1 million, which was offset by a decrease in the net loss of $4.8 million and a decrease in accrued expenses and other current liabilities of $0.9 million. In addition, there was an increase in the non-cash change in the fair value of the warrant liability of $11.4 million, an increase in non-cash stock-based compensation of $0.9 million, an increase in non-cash investment income of $0.4 million and an increase in non-cash depreciation of $0.1 million.

Net cash used in investing activities. Net cash used in investing activities was $25.1 million for the year ended December 31, 2018 compared to net cash used in investing activities of $12.4 million for the year ended December 31, 2017. The cash used in investing activities in the year ended December 31, 2018 was primarily the result of $34.9 million in proceeds from the sale of marketable securities, offset by $58.0 million for the purchase of marketable securities and $2.0 million to purchase property and equipment. The cash used in investing activities in the year ended December 31, 2017 was primarily the result of $22.3 million in proceeds from the sale of marketable securities, offset by $34.4 million for the purchase of marketable securities and $0.3 million to purchase property and equipment.

Net cash provided by financing activities. Net cash provided by financing activities was $41.2 million during the year ended December 31, 2018 compared to $43.5 million during the year ended December 31, 2017. The cash provided by financing activities in the year ended December 31, 2018 was primarily the result of $38.0 million of net proceeds received from the August 2018 public offering of common stock and $3.2 million of net proceeds from the Sales Agreement. The cash provided by financing activities in the year ended December 31, 2017 was primarily the result of $39.7 million of net proceeds received from the June 2017 public offering of common stock, $3.7 million of net proceeds from the Sales Agreement, $0.1 million for the exercise of warrants and $0.1 million from the exercise of stock options.

Funding Requirements

We expect to continue to incur significant and increasing losses for the foreseeable future. We anticipate these losses to increase as our expenses increase, and we expect that our expenses will increase if and as we:

- continue to develop and conduct clinical trials of our lead product candidate, inarigivir, including our ongoing Phase 2 ACHIEVE trial and our upcoming Phase 2 CATALYST clinical trials of inarigivir for chronic HBV;

- continue preclinical development of SB 11285, our lead STING agonist product candidate, and initiate clinical trials of SB 11285, if supported by the preclinical data;
- initiate and continue research and preclinical and clinical development efforts for our other product candidates, including SB 9225, a potential fixed-dose co-formulation product that combines inarigivir and tenofovir disoproxil fumarate;
- seek to identify and develop additional product candidates;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical trials, if any;
- establish sales, marketing, distribution and other commercial infrastructure in the future to commercialize various products for which we may obtain marketing approval, if any;
- require the manufacture and supply of larger quantities of product candidates for clinical development and potentially commercialization;
- maintain, expand and protect our intellectual property portfolio;
- hire and retain additional personnel, including clinical, quality control and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and help us comply with our obligations as a public company; and
- add equipment and physical infrastructure to support our research and development programs.

We expect that our existing cash, cash equivalents and marketable securities as of December 31, 2018 will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2021. We have based this estimate on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates. Our future capital requirements both near and long-term, will depend on many factors, including, but not limited to:

- initiation, progress, timing, costs and results of clinical trials evaluating inarigivir and SB 9225;
- initiation, progress, timing, costs and results of preclinical studies and clinical trials, if applicable, of SB 11285;
- initiation, progress, timing, costs and results of preclinical studies and clinical trials of any other product candidates we may develop;
- our obligation to make royalty and non-royalty sublicense payments to third-party licensors, if any, under our licensing agreements;
- the timing, receipt, and amount of milestone payments or royalties, if any, from inarigivir, SB 11285, SB 9225 or any of our other product candidates;
- the number and characteristics of product candidates that we discover or in-license and develop;
- the outcome, timing and cost of seeking regulatory review by the FDA and comparable foreign regulatory authorities, including the potential for the FDA or comparable foreign regulatory authorities to require that we perform more studies than those we currently expect;
- the costs of filing, prosecuting, defending and enforcing any patent claims and maintaining and enforcing other intellectual property rights;
- subject to receipt of marketing approval, revenue, if any, received from commercial sales of inarigivir and any other products;
- the costs and timing of the implementation of commercial-scale manufacturing activities;

- the costs and timing of establishing sales, marketing and distribution capabilities for any product candidates for which we may receive regulatory approval; and

- the costs of operating as a public company.

Identifying potential product candidates and conducting preclinical testing 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 marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if ever. Accordingly, we will need to obtain substantial additional funds to achieve our business objectives.

Adequate additional funds may not be available to us on acceptable terms, or at all. We do not currently have any committed external source of funds. As of December 31, 2018, we had up to $59.6 million in securities available for future issuance under the S-3 Registration Statement, which included $42.7 million in shares issuable pursuant to our at-the-market program and our Sales Agreement with Cantor. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Additional debt financing and 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 and may require the issuance of warrants, which could potentially dilute the ownership interests of our stockholders.

If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, 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 programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations at December 31, 2018, and the effects such obligations are expected to have on our liquidity and cash flow in future periods (in thousands):

	Payments Due by Period				
	Total	Less Than 1 Year	1 – 3 Years	3 – 5 Years	More than 5 Years
Operating lease commitments	$ 4,830	$ 417	$ 1,096	$ 1,387	$ 1,930
Total	$ 4,830	$ 417	$ 1,096	$ 1,387	$ 1,930

In addition to the amounts shown in the above table, we have contractual obligations pursuant to our amended and restated license agreement with BioHEP. Under this agreement, we have agreed to pay up to $3.5 million in development and regulatory milestone payments to BioHEP for each distinct viral indication for which we develop licensed product(s). BioHEP is also eligible to receive tiered royalties in the low-to-mid single-digits on net product sales of licensed products by us and our affiliates and sub licensees, and a specified share of non-royalty sublicensing revenues we and our affiliates receive from sub licensees, which share of sublicensing revenues is capped at a maximum aggregate of $2.0 million under all such sublicenses. Milestone and royalty payments associated with our amended and restated license agreement with BioHEP have not been included in the above table of contractual obligations as we cannot reasonably estimate if or when they will occur. As of December 31, 2018, there have been no milestone or royalty payments made to BioHEP.

In October 2017, we entered into a lease agreement for our new principal office and laboratory space. The initial term of the lease is 125 months beginning on June 1, 2018, the date we began occupying the new premises. Following an 11-month rent abatement period, we will be obligated to make monthly rent payments in the amount of $34,699, which is subject to increase by approximately 3% annually for the first five years of the lease and by approximately 2.5% annually thereafter. The total lease payments due during the term of the lease are approximately $4.4 million and are included in the chart above. In addition, we are responsible under the lease for specified costs and charges, including certain operating expenses, utilities, taxes and insurance.

We enter into contracts in the normal course of business with third party service providers for clinical trials, preclinical research studies and testing, manufacturing and other services and products for operating purposes. We have not included our payment obligations under these contracts in the table as these contracts generally provide for termination upon notice, and therefore, we believe that our non-cancelable obligations under these agreements are not material and we cannot reasonably estimate the timing of if

and when they will occur. We could also enter into additional research, manufacturing, supplier and other agreements in the future, which may require up-front payments and even long-term commitments of cash.

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

In May 2014, the Financial Accounting Standards Board, or FASB, issued ASU 2014-09, *Revenue from Contracts with Customers* (Topic 606), which clarifies the principles for recognizing revenue and develops a common revenue standard for U.S. GAAP and International Financial Reporting Standards, or IFRS. This standard removes inconsistencies and limitations between U.S. GAAP and IFRS in revenue requirements, provides a more robust framework for addressing revenue issues, improves comparability of revenue recognition practices across entities, industries, jurisdictions, and capital markets, provides more useful information to users of financial statements through improved disclosure requirements, and simplifies the preparation of financial statements by reducing the number of requirements to which an entity must refer. Entities can transition to the standard either retrospectively or as a cumulative-effect adjustment as of the date of adoption. This update is effective for annual periods beginning after December 15, 2017, including interim periods within that reporting period and early application is not permitted. We adopted this standard as of January 1, 2018; however, until we expect material revenue to be recognized, the adoption of this standard is not expected to have an impact on our consolidated financial statements.

In January 2016, the FASB issued ASU 2016-01, *Recognition and Measurement of Financial Assets and Financial Liabilities*, which amends Accounting Standards Codification, or ASC, Subtopic 825-10, *Financial Instruments - Overall*, and includes updates on certain aspects of recognition, measurement, presentation and disclosure of financial instruments and applies to all entities that hold financial assets or owe financial liabilities. The new standard is effective for our annual period beginning after December 15, 2017, with early adoption permitted. We adopted this standard as of January 1, 2018; however, the adoption of this standard does not have an impact on our consolidated financial statements.

In September 2016, the FASB issued ASU 2016-15, *Classification of Certain Cash Receipts and Cash Payments*, which amends ASC Topic 230, *Statement of Cash Flows*, and includes provisions intended to reduce diversity in practice and provides guidance on eight specific statements of cash flows classification issues. The new standard is effective for our annual period ending after December 15, 2017, and for annual and interim periods thereafter, with early adoption permitted. We adopted this standard as of January 1, 2018; however, the adoption of this standard did not have an impact on our consolidated financial statements.

In February 2016, the FASB issued ASU No. 2016-02, *Leases* ("ASU 2016-02"). ASU 2016-02 will require lessees to recognize most leases on their balance sheet as a right-of-use asset and a lease liability. Leases will be classified as either operating or finance, and classification will be based on criteria similar to current lease accounting, but without explicit bright lines. In July 2018, the FASB issued ASU No. 2018-10, *"Codification Improvements to Topic 842, Leases"* ("ASU 2018-10"), which provides narrow amendments to clarify how to apply certain aspects of the new lease standard, and ASU No. 2018-11, "Leases (Topic 842) – Targeted Improvements" (ASU 2018-11), which addresses implementation issues related to the new lease standard. The guidance is effective for annual reporting periods beginning after December 15, 2018 and interim periods within those fiscal years, and early adoption is permitted. Under this standard, disclosures are required to enable users of financial statements in assessing the amount, timing, and uncertainty of cash flows arising from leases. The standard permits two transition methods, (1) to apply the new lease requirements at the beginning of the earliest period presented, or (2) to apply the new lease requirements at the effective date. Under both transition methods there is a cumulative effect adjustment.

We adopted the standard on the effective date of January 1, 2019 by applying the new lease requirements at the effective date. We also elected the package of practical expedients permitted under the transition guidance within the new standard, which, among other things, allows us to carry forward the historical lease classification. We are currently evaluating the potential changes from this ASU to our future financial reporting and disclosures and designing and implementing related processes and controls. We expect the standard to have an impact of approximately $3.0 million on our assets and $3.4 million on our liabilities for the recognition of right-of-use-assets and lease liabilities, which are primarily related to the lease of our corporate headquarters in Hopkinton, Massachusetts. We do not expect the standard to have a material impact on our results of operations or liquidity.

In July 2017, the FASB issued ASU 2017-11, *Earnings Per Share (Topic 260), Distinguishing Liabilities from Equity (Topic 480), Derivatives and Hedging (Topic 815): I. Accounting for Certain Financial Instruments with Down Round Features and II. Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception.* Part I applies to entities that issue financial instruments

such as warrants, convertible debt or convertible preferred stock that contain down round features. Part II simply replaces the indefinite deferral for certain mandatorily redeemable noncontrolling interests and mandatorily redeemable financial instruments of nonpublic entities contained within Accounting Standards Codification ("ASC") Topic 480 with a scope exception and does not impact the accounting for these mandatorily redeemable instruments. This ASU is effective for public companies for the annual reporting periods beginning after December 15, 2018, and interim periods within those annual periods. Early adoption is permitted. We adopted this standard as of January 1, 2019; however, the adoption of this standard did not impact our consolidated financial statements.

In June 2018, the FASB issued ASU 2018-07, *Improvements to Nonemployee Share-Based Payment Accounting*, which amends ASC Topic 718, *Compensation – Stock Compensation*, and includes provisions intended to provide simplification of several aspects of accounting for nonemployee share-based payment transactions. The new standard is effective for us for the annual period beginning after December 15, 2018, including interim periods within that fiscal year. Early adoption is permitted, but no earlier than the date on which we adopted Topic 606. We elected early adoption of this standard as of September 30, 2018. The adoption of this standard has resulted in a de minimis impact on our consolidated financial statements.

Other accounting standards that have been issued or proposed by the FASB or other standards-setting bodies that do not require adoption until a future date are not expected to have a material impact on our consolidated financial statements upon adoption.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risk related to changes in interest rates. Our cash, cash equivalents and marketable securities of $64.4 million as of December 31, 2018, consisted of cash, cash equivalents and marketable securities. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. However, because a significant amount of the marketable securities in our investment portfolio are short-term in nature , an immediate 10% change in market interest rates would not be expected to have a material impact on the fair market value of our investment portfolio or on our financial condition or results of operations.

Item 8. Financial Statements and Supplementary Data.

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K. An index of those financial statements is found in Item 15.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and our principal financial officer, evaluated, as of the end of the period covered by this Annual Report on Form 10-K, the effectiveness of our disclosure controls and procedures. Based on that evaluation of our disclosure controls and procedures as of December 31, 2018, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures as of such date are effective at the reasonable assurance level. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act are recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports we file or submit under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial and accounting officer, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Inherent Limitations of Internal Controls

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) under the Securities Exchange Act of 1934, as amended, as a process designed by, or under the supervision of, the Company's principal executive and principal financial officers and effected by the company's board of directors, management and other personnel to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- Pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the Company;
- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures are being made only in accordance with authorizations of management and directors of the Company; and
- Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company's assets that could have a material effect on the financial statements.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2018. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO") in Internal Control-Integrated Framework (2013).

Based on our assessment, management believes that, as of December 31, 2018, our internal control over financial reporting is effective based on those criteria.

As an "emerging growth company" under the Jumpstart Our Business Startups Act, we are exempt from the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002. As a result, RSM US LLP, our independent registered public accounting firm, has not audited or issued an attestation report with respect to the effectiveness of our internal control over financial reporting as of December 31, 2018.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the fourth quarter ended December 31, 2018, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Management and Corporate Governance," "Section 16(a) Beneficial Ownership Reporting Compliance," and "Code of Business Conduct and Ethics" in our proxy statement for the 2019 annual meeting of stockholders.

Item 11. Executive Compensation.

The response to this item is incorporated by reference from the discussion responsive thereto under the caption "Executive Officer and Director Compensation" in our proxy statement for the 2019 annual meeting of stockholders.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information" in our proxy statement for the 2019 annual meeting of stockholders.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Certain Relationships and Related Person Transactions" and "Management and Corporate Governance" in our proxy statement for the 2019 annual meeting of stockholders.

Item 14. Principal Accounting Fees and Services.

The response to this item is incorporated by reference from the discussion responsive thereto under the caption "Ratification of Selection of Independent Registered Public Accounting Firm" in our proxy statement for the 2019 annual meeting of stockholders.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) The following documents are filed as part of this report:

(1) Financial Statements:

(2) Financial Statement Schedules:

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

(3) Exhibits. The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference Herein from Form or Schedule	Filing Date	SEC File/Reg. Number
3.1	Restated Certificate of Incorporation of the Registrant		Form 8-K (Exhibit 3.1)	May 13, 2016	001-37718
3.2	Amended and Restated Bylaws of the Registrant		Form 8-K (Exhibit 3.2)	May 13, 2016	001-37718
4.1	Specimen stock certificate evidencing the shares of common stock		Form S-1/A (Exhibit 4.1)	February 12, 2016	333-208875
4.2	Form of Warrant issued to Dawson James Securities, Inc. (May 2016)		Form 8-K (Exhibit 10.1)	May 13, 2016	001-37718
4.3	Form of Warrant to Purchase Common Stock (November 2016)		Form 8-K (Exhibit 10.2)	November 21, 2016	001-37718
10.1	Form of Indemnification Agreement between Registrant and each of its directors and officers		Form S-1 (Exhibit 10.1)	January 5, 2016	333-208875
10.2#	2014 Stock Incentive Plan		Form S-1 (Exhibit 10.2)	January 5, 2016	333-208875
10.3#	Form of Incentive Stock Option Agreement under 2014 Stock Incentive Plan		Form S-1 (Exhibit 10.3)	January 5, 2016	333-208875

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference Herein from Form or Schedule	Filing Date	SEC File/Reg. Number
10.4#	Form of Nonstatutory Stock Option Agreement under 2014 Stock Incentive Plan		Form S-1 (Exhibit 10.4)	January 5, 2016	333-208875
10.5#	Spring Bank Pharmaceuticals, Inc. Amended and Restated 2015 Stock Incentive Plan.		Form 8-K (Exhibit 10.1)	June 19, 2018	333-208875
10.6#	Form of Incentive Stock Option Agreement under 2015 Stock Incentive Plan		Form S-1 (Exhibit 10.6)	January 5, 2016	333-208875
10.7#	Form of Nonstatutory Stock Option Agreement under 2015 Stock Incentive Plan		Form S-1 (Exhibit 10.7)	January 5, 2016	333-208875
10.8#	Form of Performance-Based Restricted Stock Unit Agreement under 2015 Stock Incentive Plan	X			
10.9	Lease Agreement between 35 Parkwood Realty LLC and Spring Bank Pharmaceuticals, Inc., dated October 4, 2017		Form 8-K (Exhibit 10.1)	October 5, 2017	001-37718
10.9.1	Amendment No. 1 to Lease Agreement between 35 Parkwood Realty LLC and Spring Bank Pharmaceuticals, Inc., dated August 10, 2018.		Form 10-Q (Exhibit 10.1)	October 25, 2018	001-37718
10.10	Lease Agreement between the Registrant and JEEBO Management, LLC, dated March 24, 2016, as amended March 31, 2016		Form S-1/A (Exhibit 10.19)	April 27, 2016	333-208875
10.11†	Amended and Restated License Agreement between Registrant and BioHEP Technologies Ltd. (formerly known as Micrologix Biotech Inc.), dated January 14, 2016		Form S-1/A (Exhibit 10.9)	January 15, 2016	333-208875
10.12#	Employment Agreement between Registrant and R.P. Kris Iyer, Ph.D. dated December 16, 2015		Form S-1 (Exhibit 10.10)	January 5, 2016	333-208875
10.13#	Employment Agreement between Registrant and Martin Driscoll dated August 7, 2015		Form S-1 (Exhibit 10.14)	January 5, 2016	333-208875
10.14#	Employment Agreement between Registrant and Jonathan P. Freve dated December 1, 2015		Form S-1 (Exhibit 10.15)	January 5, 2016	333-208875
10.15#	Employment Agreement between Registrant and Nezam H. Afdhal, M.D. dated November 1, 2015		Form S-1 (Exhibit 10.16)	January 5, 2016	333-208875
10.16	Securities Purchase Agreement, dated November 18, 2016, by and among the Registrant and the persons party thereto		Form 8-K (Exhibit 10.1)	November 21, 2016	001-37718

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference Herein from Form or Schedule	Filing Date	SEC File/Reg. Number
10.17	Registration Rights Agreement, dated November 18, 2016, by and among the Registrant and the persons party thereto		Form 8-K (Exhibit 10.3)	November 21, 2016	001-37718
10.18	Non-Employee Director Compensation Policy		Form 10-K (Exhibit 10.18)	February 14, 2017	001-37718
10.18.1	Amended and Restated Non-Employee Director Compensation Policy, effective January 1, 2019	X			
10.19	Controlled Equity Offering℠ Sales Agreement by and between the Registrant and Cantor Fitzgerald & Co., dated August 18, 2017		Form 8-K (Exhibit 10.1)	August 18, 2017	001-37718
21.1	Subsidiaries of the Registrant		Form 10-K (Exhibit 21.1)	February 14, 2017	001-37718
23.1	Consent of RSM US LLP	X			
31.1	Certification of Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	X			
31.2	Certification of Principal Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	X			
32.1	Certification pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, by Chief Executive Officer and Principal Financial Officer	X			
101.INS	XBRL Instance Document	X			
101.SCH	XBRL Taxonomy Extension Schema Document	X			
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	X			
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document	X			
101.LAB	XBRL Taxonomy Extension Label Linkbase Document	X			
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document	X			

# Indicates management contract or compensatory plan

† Confidential treatment granted as to portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

Item 16. Form 10-K Summary.

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

Spring Bank Pharmaceuticals, Inc.

Date: March 11, 2019

By: /s/ Martin Driscoll
Martin Driscoll
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this report has been signed below by the following persons on behalf of the registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Martin Driscoll **Martin Driscoll**	President and Chief Executive Officer (Principal Executive Officer)	March 11, 2019
/s/ Jonathan Freve **Jonathan Freve**	Chief Financial Officer and Treasurer (Principal Financial and Accounting Officer)	March 11, 2019
/s/ Radhakrishnan Iyer, Ph.D. **Radhakrishnan Iyer, Ph.D.**	Chief Scientific Officer and Director	March 11, 2019
/s/ Scott Smith **Scott Smith**	Chairman of the Board and Director	March 11, 2019
/s/ David Arkowitz **David Arkowitz**	Director	March 11, 2019
/s/ Todd Brady, M.D., Ph.D. **Todd Brady, M.D., Ph.D.**	Director	March 11, 2019
/s/ Timothy Clackson, Ph.D. **Timothy Clackson, Ph.D.**	Director	March 11, 2019
/s/ Kurt Eichler **Kurt Eichler**	Director	March 11, 2019

SRING BANK PHARMACEUTICALS, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

SPRING BANK PHARMACEUTICALS, INC.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of
Spring Bank Pharmaceuticals, Inc.
Hopkinton, Massachusetts

Opinion on the Financial Statements
We have audited the accompanying consolidated balance sheets of Spring Bank Pharmaceuticals, Inc. and its subsidiaries (the Company) as of December 31, 2018 and 2017, the related consolidated statements of operations and comprehensive loss, changes in stockholders' equity and cash flows for the years then ended, and the related notes to the consolidated financial statements (collectively, the financial statements). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for the years then ended, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion
These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ RSM US LLP

We have served as the Company's auditor since 2013.

Boston, Massachusetts
March 11, 2019

SPRING BANK PHARMACEUTICALS, INC.

CONSOLIDATED BALANCE SHEETS
(In Thousands, Except Share and Per Share Data)

	December 31, 2018	December 31, 2017
ASSETS		
Current assets:		
Cash and cash equivalents	$ 14,724	$ 23,649
Marketable securities	32,914	26,906
Prepaid expenses and other current assets	1,649	580
Total current assets	49,287	51,135
Marketable securities, long-term	16,804	—
Property and equipment, net	2,319	687
Restricted cash	234	484
Other assets	167	35
Total	$ 68,811	$ 52,341
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 1,880	$ 1,700
Accrued expenses and other current liabilities	2,367	2,734
Total current liabilities	4,247	4,434
Warrant liabilities	8,511	13,128
Other long-term liabilities	193	31
Total liabilities	12,951	17,593
Commitments and contingencies (Note 9)		
Stockholders' equity:		
Preferred stock, $0.0001 par value—authorized, 10,000,000 shares at December 31, 2018 and 2017; no shares issued or outstanding at December 31, 2018 and 2017	—	—
Common stock, $0.0001 par value—authorized, 200,000,000 shares at December 31, 2018 and 2017; 16,434,614 and 12,961,993 shares issued and outstanding outstanding at December 31, 2018 and 2017, respectively	2	1
Additional paid-in capital	157,931	113,984
Accumulated deficit	(102,068)	(79,214)
Other comprehensive loss	(5)	(23)
Total stockholders' equity	55,860	34,748
Total	$ 68,811	$ 52,341

See accompanying notes to consolidated financial statements.

SPRING BANK PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In Thousands, Except Share and Per Share Data)

	Year Ended December 31,	
	2018	2017
Operating expenses:		
Research and development	$ 19,751	$ 13,075
General and administrative	8,719	8,178
Total operating expenses	28,470	21,253
Loss from operations	(28,470)	(21,253)
Other income (expense):		
Interest income	999	369
Change in fair value of warrant liabilities	4,617	(6,795)
Net loss	(22,854)	(27,679)
Unrealized gain (loss) on marketable securities	18	(16)
Comprehensive loss	$ (22,836)	$ (27,695)
Net loss per common share:		
Basic	$ (1.59)	$ (2.48)
Diluted	$ (1.88)	$ (2.48)
Weighted-average number of shares outstanding:		
Basic	14,372,174	11,153,269
Diluted	14,618,976	11,153,269

See accompanying notes to consolidated financial statements.

SPRING BANK PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY
(In Thousands, Except Share and Per Share Data)

	Common Stock		Additional Paid-in	Accumulated	Other Comprehensive	Total Stockholders'
	Shares	Amount	Capital	Deficit	Income (loss)	Equity
Balance at December 31, 2016	9,416,238	$ 1	$ 68,559	$ (51,535)	$ (7)	$ 17,018
Stock-based compensation	—	—	1,840	—	—	1,840
Issuance of common stock for services rendered	3,133	—	47	—	—	47
Exercise of warrants	10,960	—	118	—	—	118
Exercise of stock options	10,000	—	92	—	—	92
Issuance of common stock in connection with offering, net of issuance costs of $2,826	3,269,219	—	39,675	—	—	39,675
Issuance of common stock in connection with at-the-market offering, net of issuance costs of $273	252,443	—	3,653	—	—	3,653
Net unrealized loss on marketable securities	—	—	—	—	(16)	(16)
Net loss	—	—	—	(27,679)	—	(27,679)
Balance at December 31, 2017	12,961,993	$ 1	$113,984	$ (79,214)	$ (23)	$ 34,748
Stock-based compensation	—	—	2,662	—	—	2,662
Issuance of common stock for services rendered	9,213	—	114	—	—	114
Issuance of common stock in connection with offering, net of issuance costs of $2,618	3,246,079	1	37,959	—	—	37,960
Issuance of common stock in connection with at-the-market offering, net of issuance costs of $140	217,329	—	3,212	—	—	3,212
Net unrealized gain on marketable securities	—	—	—	—	18	18
Net loss	—	—	—	(22,854)	—	(22,854)
Balance at December 31, 2018	16,434,614	$ 2	$157,931	$ (102,068)	$ (5)	$ 55,860

See accompanying notes to consolidated financial statements.

SPRING BANK PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(In Thousands)

	Year Ended December 31, 2018	2017
Cash flows from operating activities:		
Net loss	$ (22,854)	$ (27,679)
Adjustments for:		
Depreciation and amortization	288	158
Loss on disposal of property and equipment	52	—
Change in fair value of warrant liabilities	(4,617)	6,795
Non-cash investment income (expense)	337	(41)
Non-cash stock-based compensation	2,776	1,911
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(1,069)	260
Other assets	(132)	—
Accounts payable	180	181
Accrued expenses and other liabilities	(205)	732
Net cash used in operating activities	(25,244)	(17,683)
Cash flows from investing activities:		
Purchases of marketable securities	(58,000)	(34,397)
Proceeds from sale of marketable securities	34,869	22,314
Purchases of property and equipment	(1,972)	(323)
Net cash used in investing activities	(25,103)	(12,406)
Cash flows from financing activities:		
Proceeds from issuance of common stock, net of issuance costs	37,960	39,675
Proceeds from issuance of common stock in connection with at-the-market offering, net of issuance costs	3,212	3,653
Proceeds from exercise of warrants	—	118
Proceeds from exercise of stock options	—	92
Cash provided by financing activities	41,172	43,538
Net (decrease) increase in cash, cash equivalents and restricted cash	(9,175)	13,449
Cash, cash equivalents and restricted cash, beginning of period	24,133	10,684
Cash, cash equivalents and restricted cash, end of period	$ 14,958	$ 24,133
Supplemental disclosures of cash flow information:		
Cash paid for taxes	$ 3	$ 1
Cash paid for interest, net	$ —	$ —

See accompanying notes to consolidated financial statements.

1. NATURE OF BUSINESS, BASIS OF PRESENTATION AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Nature of Business

Spring Bank Pharmaceuticals, Inc. (the "Company") is a clinical-stage biopharmaceutical company engaged in the discovery and development of a novel class of therapeutics using a proprietary small molecule nucleotide platform. The Company is developing its most advanced product candidate, inarigivir soproxil ("inarigivir"), for the treatment of chronic hepatitis B virus. Since inception in 2002 and prior to its initial public offering ("IPO") in May 2016, the Company built its technology platform and product candidate pipeline, supported by grants and through private financings. In September 2015, the Company formed a wholly owned subsidiary, Sperovie Biosciences, Inc., and in December 2016, the Company formed a wholly owned subsidiary, SBP Securities Corporation.

The Company's success is dependent upon its ability to successfully complete clinical development and obtain regulatory approval of its product candidates, successfully commercialize approved products, generate revenue, and, ultimately, attain profitable operations. The Company's operations to date have been primarily limited to the development of inarigivir, SB 11285, SB 9225 and the Company's other product candidates.

Basis of Presentation and Liquidity

The accompanying consolidated financial statements have been prepared in accordance with United States ("U.S.") generally accepted accounting principles ("U.S. GAAP").

As of December 31, 2018, the Company had an accumulated deficit of $102.1 million and $64.4 million in cash, cash equivalents and marketable securities.

The Company expects to continue to incur significant and increasing losses for the foreseeable future. The Company anticipates that its expenses will increase significantly as it continues to develop inarigivir, SB 11285, SB 9225 and its other product candidates. The Company does not have any committed external source of funds. As a result, the Company will need additional financing to support its continuing operations. Adequate additional funds may not be available to the Company on acceptable terms, or at all. To the extent that the Company raises additional capital through the sale of equity or convertible debt securities, stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect common stockholder rights. If the Company raises additional funds through collaborations, strategic alliances or licensing arrangements with third parties, the Company may have to relinquish valuable rights to its technologies, future revenue streams, research programs, or product candidates or grant licenses on terms that may not be favorable to the Company.

Principles of Consolidation

The consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries, Sperovie Biosciences, Inc. and SBP Securities Corporation. Sperovie Biosciences, Inc. had operations consisting mainly of legal fees associates with intellectual property activities as of December 31, 2018. SBP Securities Corporation had assets primarily related to investments in marketable securities and operations consisting primarily of interest income as of December 31, 2018. All intercompany balances and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. The Company bases estimates and assumptions on historical experience when available and on various factors that it believes to be reasonable under the circumstances. Significant estimates relied upon in preparing the accompanying financial statements related to the fair value of marketable securities, common stock and warrant liabilities, accounting for stock-based compensation, income taxes, useful lives of long-lived assets, and accounting for certain accruals. The Company evaluates its estimates and assumptions on an ongoing basis. The Company's actual results may differ from these estimates.

Cash and Cash Equivalents

Cash equivalents are stated at fair value and include short-term, highly liquid investments with remaining maturities of 90 days or less at the date of purchase. Included in cash and cash equivalents as of December 31, 2018 are money market fund investments of $13.3 million. As of December 31, 2017, included in cash and cash equivalents are money market fund investments of $21.3 million, which are reported at fair value (Note 5).

Restricted Cash

As of December 31, 2018, restricted cash consisted of approximately $234,000, which is held as a security deposit required in conjunction with the lease agreement entered into in October 2017. As of December 31, 2017, restricted cash consisted of approximately $484,000, of which $250,000 is held as collateral for the Company's credit card program and $234,000 is held as a security deposit required in conjunction with a lease agreement entered into in October 2017.

Concentration of Credit Risk

Financial instruments that subject the Company to significant concentrations of credit risk consist primarily of cash, cash equivalents, restricted cash and marketable securities. Substantially all of the Company's cash is held at financial institutions that management believes to be of high-credit quality. Deposits with these financial institutions may exceed the amount of insurance provided on such deposits; however, these deposits may be redeemed upon demand and, therefore, bear minimal risk.

Investments in Marketable Securities

The Company invests excess cash balances in short-term and long-term marketable securities. The Company classifies investments in marketable securities as either held-to-maturity or available-for-sale based on facts and circumstances present at the time of purchase. At each balance sheet date presented, all investments in securities are classified as available-for-sale. The Company reports available-for-sale investments at fair value at each balance sheet date and includes any unrealized holding gains and losses (the adjustment to fair value) in accumulated other comprehensive income (loss), a component of stockholders' equity. Realized gains and losses are determined using the specific identification method and are included in other income (expense). If any adjustment to fair value reflects a decline in the value of the investment, the Company considers all available evidence to evaluate the extent to which the decline is "other than temporary," including the intention to sell and, if so, marks the investment to market through a charge to the Company's consolidated statements of operations and comprehensive loss.

Property and Equipment, Net

Property and equipment are recorded at cost. Costs associated with maintenance and repairs are expensed as incurred. Depreciation and amortization are provided using the straight-line method over the estimated useful lives:

Asset Category	Useful Life
Equipment	5-7 years
Furniture and fixtures	5 years
Leasehold improvements	Lesser of 10 years or the remaining term of the respective lease

Impairment of Long-Lived Assets

Long-lived assets to be held and used are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of the asset may not be recoverable. When such events occur, the Company compares the carrying amounts of the assets to their undiscounted expected future cash flows. If the undiscounted cash flows are insufficient to recover the carrying value, an impairment loss is recorded for the difference between the carrying value and fair value of the asset. Through December 31, 2018, no such impairment has occurred.

Deferred Rent

The Company's operating leases include rent escalation payment terms and other incentives received from landlords. Deferred rent represents the difference between actual operating lease payments due and straight-line rent expense over the term of the lease, which is recorded in accrued expenses and other current liabilities. The Company had deferred aggregate rent of $249,000 and $35,000 as of December 31, 2018 and 2017, respectively.

Research and Development Costs

Research and development expenses consist primarily of costs incurred for the Company's research activities, including discovery efforts, and the development of product candidates, which include:

- expenses incurred under agreements with third parties, including contract research organizations, or CROs, that conduct research, preclinical activities and clinical trials on the Company's behalf as well as contract manufacturing organizations, or CMOs, that manufacture drug products for use in the Company's preclinical and clinical trials;
- salaries, benefits and other related costs, including stock-based compensation expense, for personnel in the Company's research and development functions;
- costs of outside consultants, including their fees, stock-based compensation and related travel expenses;
- the cost of laboratory supplies and acquiring, developing and manufacturing preclinical study and clinical trial materials;
- costs related to compliance with regulatory requirements; and
- facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

The Company expenses research and development costs as incurred. The Company recognizes external development costs based on an evaluation of the progress to completion of specific tasks using information provided to the Company by its vendors and its clinical investigative sites. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in the Company's consolidated financial statements as prepaid or accrued research and development expenses.

Warrants

The Company reviews the terms of all warrants issued and classifies the warrants as a component of permanent equity if they are freestanding financial instruments that are legally detachable and separately exercisable, contingently exercisable, do not embody an obligation for the Company to repurchase its own shares, and permit the holders to receive a fixed number of shares of common stock upon exercise. In addition, the warrants must require physical settlement and may not provide any guarantee of value or return. Warrants that meet these criteria are initially recorded at their grant date fair value and are not subsequently remeasured. Warrants that do not meet this criteria are classified as liabilities and remeasured to their fair value at each reporting period.

Stock-Based Compensation

The Company accounts for all stock-based payment awards granted to employees and nonemployees using a fair value method. The Company's stock-based payments include stock options and grants of common stock, including common stock subject to vesting. The measurement date for employee awards is the date of grant, and stock-based compensation costs are recognized as expense over the employees' requisite service period, which is generally the vesting period, on a straight-line basis. The Company adopted ASU 2018-07, *Improvements to Nonemployee Share-Based Payment Accounting*, effective July 1, 2018, which aligns the accounting treatment of nonemployee awards with employee awards. Stock-based compensation expense is classified in the accompanying consolidated statements of operations and comprehensive loss based on the department to which the related services are provided.

Financial Instruments

The Company's financial instruments consisted of cash equivalents, marketable securities, accounts payable and liability classified warrants. The carrying amounts of cash and cash equivalents and accounts payable approximate their fair value due to the short-term nature of those financial instruments. The fair value of the marketable securities and liability classified warrants are remeasured to fair value each reporting period as described in Note 5.

Fair Value Measurements

The Company is required to disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values. Accounting Standards Codification 820, *Fair Value Measurements and Disclosures* ("ASC 820"), establishes a hierarchy of inputs used when available. Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability and are developed based on the best information available in the circumstances. The fair value hierarchy applies only to the valuation inputs used in determining the reported fair value of the investments and is not a measure of the investment credit quality. The three levels of the fair value hierarchy are described below:

Level 1 – Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date.

Level 2 – Valuations based on quoted prices for similar assets or liabilities in markets that are not active or for which all significant inputs are observable, either directly or indirectly.

Level 3 – Valuations that require inputs that reflect the Company's own assumptions that are both significant to the fair value measurement and unobservable.

To the extent that valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement. The Company's assets and liabilities measured at fair value on a recurring basis include cash equivalents, marketable securities and warrant liabilities.

Net Loss Per Share

Basic net loss per share is computed by dividing the net loss by the weighted-average number of shares of common stock outstanding for the period. Diluted net loss per share is computed by dividing the net loss by the weighted-average number of shares of common stock and dilutive common stock equivalents outstanding for the period, determined using the treasury-stock method and the as if-converted method, for convertible securities, if inclusion of these instruments is dilutive. For the year ended December 31, 2018, diluted net loss per share amounts were calculated based on the dilutive effect of the total number of shares of common stock related to the November 2016 Private Placement Warrants and the change in the fair value of the warrant liability. As of December 31, 2017, both methods are equivalent. Basic and diluted net loss per share is described further in Note 2.

Income Taxes

Deferred tax assets and liabilities are determined based upon the differences between the financial statement carrying amounts and the tax basis of existing assets and liabilities and for loss and credit carryforwards using enacted tax rates expected to be in effect in the years in which the differences are expected to reverse. Deferred tax assets are reduced by a valuation allowance if it is more likely than not that some portion or all of the deferred tax asset will not be realized.

The Company assesses its income tax positions and records tax benefits based upon management's evaluation of the facts, circumstances, and information available at the reporting date. For those tax positions where it is more likely than not that a tax benefit will be sustained, the Company records the largest amount of tax benefit with a greater than 50% likelihood of being realized upon ultimate settlement with a taxing authority having full knowledge of all relevant information. For those income tax positions where it is not more likely than not that a tax benefit will be sustained, no tax benefit is recognized in the consolidated financial statements. The Company classifies interest and penalties associated with such uncertain tax positions as a component of interest expense. As of December 31, 2018 and 2017, the Company has not identified any material uncertain tax positions.

Guarantees and Indemnifications

As permitted under Delaware law, the Company indemnifies its officers and directors for certain events or occurrences while the officer or director is, or was, serving at the Company's request in such capacity.

The Company leases office and laboratory space in Hopkinton, Massachusetts and previously leased research and development space in Milford, Massachusetts under non-cancelable operating leases. The Company has standard indemnification arrangements under these leases that require it to indemnify the landlords against liability for injury, loss, accident, or damage from any claims, actions, proceedings, or costs resulting from certain acts, breaches, violations, or nonperformance under the Company's lease.

Through December 31, 2018, the Company had not experienced any losses related to these indemnification obligations and no material claims were outstanding. The Company does not expect significant claims related to these indemnification obligations, and consequently, concluded that the fair value of these obligations is negligible, and no related reserves were established.

Segment Information

Operating segments are identified as components of an enterprise about which separate and discrete financial information is available for evaluation by the chief operating decision maker, the Company's Chief Executive Officer, in making decisions regarding resource allocation and assessing performance. The Company views its operations and manages its business in one operating segment and does not track expenses on a program-by-program basis.

Recently Issued Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board, or FASB, issued ASU 2014-09, *Revenue from Contracts with Customers* (Topic 606), which clarifies the principles for recognizing revenue and develops a common revenue standard for U.S. GAAP and International Financial Reporting Standards, or IFRS. This standard removes inconsistencies and limitations between U.S. GAAP and IFRS in revenue requirements, provides a more robust framework for addressing revenue issues, improves comparability of revenue recognition practices across entities, industries, jurisdictions, and capital markets, provides more useful information to users of financial statements through improved disclosure requirements, and simplifies the preparation of financial statements by reducing the number of requirements to which an entity must refer. Entities can transition to the standard either retrospectively or as a cumulative-effect adjustment as of the date of adoption. This update is effective for annual periods beginning after December 15, 2017, including interim periods within that reporting period and early application is not permitted. The Company adopted this standard as of January 1, 2018; however, until the Company expects material revenue to be recognized, the adoption of this standard is not expected to have an impact on the Company's consolidated financial statements.

In January 2016, the FASB issued ASU 2016-01, *Recognition and Measurement of Financial Assets and Financial Liabilities*, which amends ASC Subtopic 825-10, *Financial Instruments - Overall*, and includes updates on certain aspects of recognition, measurement, presentation and disclosure of financial instruments and applies to all entities that hold financial assets or owe financial liabilities. The new standard is effective for the Company for the annual period beginning after December 15, 2017, with early adoption permitted. The Company adopted this standard as of January 1, 2018; however, the adoption of this standard did not impact the Company's consolidated financial statements.

In September 2016, the FASB issued ASU 2016-15, *Classification of Certain Cash Receipts and Cash Payments*, which amends ASC Topic 230, *Statement of Cash Flows*, and includes provisions intended to reduce diversity in practice and provides guidance on eight specific statements of cash flows classification issues. The new standard is effective for the Company for the annual period ending after December 15, 2017, and for annual and interim periods thereafter, with early adoption permitted. The Company adopted this standard as of January 1, 2018; however, the adoption of this standard did not impact the Company's consolidated financial statements.

In February 2016, the FASB issued ASU No. 2016-02, *Leases* ("ASU 2016-02"). ASU 2016-02 will require lessees to recognize most leases on their balance sheet as a right-of-use asset and a lease liability. Leases will be classified as either operating or finance, and classification will be based on criteria similar to current lease accounting, but without explicit bright lines. In July 2018, the FASB issued ASU No. 2018-10, *"Codification Improvements to Topic 842, Leases"* ("ASU 2018-10"), which provides narrow amendments to clarify how to apply certain aspects of the new lease standard, and ASU No. 2018-11, "Leases (Topic 842) – Targeted Improvements" (ASU 2018-11), which addresses implementation issues related to the new lease standard. The guidance is effective for annual reporting periods beginning after December 15, 2018 and interim periods within those fiscal years, and early adoption is permitted. Under this standard, disclosures are required to enable users of financial statements in assessing the amount, timing, and uncertainty of cash flows arising from leases. The standard permits two transition methods, (1) to apply the new lease requirements at the beginning of the earliest period presented, or (2) to apply the new lease requirements at the effective date. Under both transition methods there is a cumulative effect adjustment.

The Company adopted the standard on the effective date of January 1, 2019 by applying the new lease requirements at the effective date. The Company also elected the package of practical expedients permitted under the transition guidance within the new standard, which, among other things, allows the Company to carry forward the historical lease classification. The Company is currently evaluating the potential changes from this ASU to our future financial reporting and disclosures and designing and implementing related processes and controls. The Company expects the standard to have an impact of approximately $3.0 million on our assets and $3.4 million on our liabilities for the recognition of right-of-use-assets and lease liabilities, which are primarily related to the lease of our corporate headquarters in Hopkinton, Massachusetts. The Company does not expect the standard to have a material impact on our results of operations or liquidity.

In July 2017, the FASB issued ASU 2017-11, *Earnings Per Share (Topic 260), Distinguishing Liabilities from Equity (Topic 480), Derivatives and Hedging (Topic 815): I. Accounting for Certain Financial Instruments with Down Round Features and II. Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception.* Part I applies to entities that issue financial instruments such as warrants, convertible debt or convertible preferred stock that contain down round features. Part II simply replaces the indefinite deferral for certain mandatorily redeemable noncontrolling interests and mandatorily redeemable financial instruments of nonpublic entities contained within Accounting Standards Codification (ASC) Topic 480 with a scope exception and does not impact the accounting for these mandatorily redeemable instruments. This ASU is effective for public companies for the annual reporting periods beginning after December 15, 2018, and interim periods within those annual periods. Early adoption is permitted. The Company adopted this standard as of January 1, 2019; however, the adoption of this standard did not impact the Company's consolidated financial statements.

In June 2018, the FASB issued ASU 2018-07, *Improvements to Nonemployee Share-Based Payment Accounting*, which amends ASC Topic 718, *Compensation – Stock Compensation*, and includes provisions intended to provide simplification of several aspects of accounting for nonemployee share-based payment transactions. The new standard is effective for the Company for the annual period beginning after December 15, 2018, including interim periods within that fiscal year. Early adoption is permitted, but no earlier than the Company's adoption date of Topic 606. The Company elected early adoption of this standard as of July 1, 2018. The adoption of this standard has resulted in a de minimis impact on the Company's consolidated financial statements.

2. NET LOSS PER SHARE

The following table summarizes the computation of basic and diluted net loss per share of the Company for such periods (in thousands, except share and per share data):

	Year Ended December 31,	
	2018	2017
Net loss	$ (22,854)	$ (27,679)
Less: decrease in change in fair value of warrant liabilities	(4,617)	—
Net loss available to common shareholders	$ (27,471)	$ (27,679)
Weighted-average number of shares outstanding:		
Basic	14,372,174	11,153,269
Effect of dilutive securities:		
Common stock warrants	246,802	—
Dilutive potential common shares	14,618,976	11,153,269
Net loss per common share:		
Basic	$ (1.59)	$ (2.48)
Diluted	$ (1.88)	$ (2.48)

For the year ended December 31, 2018, the diluted net loss per common share amounts under the treasury stock method was calculated based on the dilutive effect of the total number of shares of common stock related to the November 2016 Private Placement Warrants of 1,633,777 shares with an exercise price of $10.79. For the period ended December 31, 2018, the average stock price was $12.71, providing 246,802 dilutive shares for the November 2016 Private Placement Warrants. The change in the fair value of the warrant liability of $4.6 million is included in the net loss available to common shareholders for the diluted net loss per common share amount. For the year ended December 31, 2017, the diluted net loss per common share is the same as basic net loss per common share.

The following potentially dilutive securities outstanding, prior to the use of the treasury stock method or if-converted method, have been excluded from the computation of diluted weighted-average shares outstanding, because such securities had an antidilutive impact due to the losses reported:

	Year Ended December 31,	
	2018	2017
Common stock warrants	28,347	1,787,124
Stock options	1,349,565	988,565

3. INVESTMENTS

Cash in excess of the Company's immediate requirements is invested in accordance with the Company's investments policy that primarily seeks to maintain adequate liquidity and preserve capital.

The following table summarizes the Company's investments, by category, as of December 31, 2018 and 2017 (in thousands):

	December 31, 2018	December 31, 2017
Investments - Current:		
Debt securities - available for sale	$ 32,914	$ 26,906
Total	$ 32,914	$ 26,906
Investments - Noncurrent:		
Debt securities - available for sale	$ 16,804	$ —
Total	$ 16,804	$ —

A summary of the Company's available-for-sale classified investments as of December 31, 2018 and 2017 consisted of the following (in thousands):

	At December 31, 2018			
	Cost Basis	Unrealized Gains	Unrealized Losses	Fair Value
Investments - Current:				
Corporate bonds	$ 16,028	$ —	$ (19)	$ 16,009
United States treasury securities	16,913	—	(8)	16,905
Total	$ 32,941	$ —	$ (27)	$ 32,914
Investments - Noncurrent:				
Corporate bonds	$ 4,930	$ 2	$ —	$ 4,932
United States treasury securities	11,852	20	—	11,872
Total	$ 16,782	$ 22	$ —	$ 16,804

	At December 31, 2017			
	Cost Basis	Unrealized Gains	Unrealized Losses	Fair Value
Investments - Current:				
Commercial paper	$ 9,584	$ —	$ —	$ 9,584
Corporate bonds	15,347	—	(23)	15,324
United States treasury securities	1,998	—	—	1,998
Total	$ 26,929	$ —	$ (23)	$ 26,906

The amortized cost and fair value of the Company's available-for-sale investments, by contract maturity, as of December 31, 2018 consisted of the following (in thousands):

	Amortized Cost	Fair Value
Due in one year or less	$ 32,941	$ 32,914
Due after one year through two years	16,782	16,804
Total	$ 49,723	$ 49,718

4. PROPERTY AND EQUIPMENT, NET

Property and equipment as of December 31, 2018 and 2017 consisted of the following (in thousands):

	December 31, 2018	December 31, 2017
Equipment	$ 1,064	$ 727
Furniture and fixtures	400	292
Leasehold improvements	1,347	153
Total property and equipment	2,811	1,172
Less: accumulated depreciation and amortization	(492)	(485)
Property and equipment, net	$ 2,319	$ 687

Depreciation expense for the years ended December 31, 2018 and 2017 was $288,000 and $158,000, respectively.

5. FAIR VALUE MEASUREMENTS

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 are performed in a manner to maximize the use of observable inputs and minimize the use of unobservable inputs.

The Company classified its money market funds within Level 1 because their fair values are based on their quoted market prices. The Company classified its commercial paper and fixed income securities within Level 2 because their fair values are determined using alternative pricing sources or models that utilized market observable inputs.

A summary of the assets and liabilities that are measured at fair value as of December 31, 2018 and 2017 is as follows (in thousands):

		Fair Value Measurement at December 31, 2018		
	Carrying Value	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Assets:				
Money market funds [1]	$ 13,264	$ 13,264	$ —	$ —
Fixed income securities	49,718	—	49,718	—
Total	$ 62,982	$ 13,264	$ 49,718	$ —
Liabilities:				
Warrant liabilities	$ 8,511	$ —	$ —	$ 8,511
Total	$ 8,511	$ —	$ —	$ 8,511

		Fair Value Measurement at December 31, 2017		
	Carrying Value	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Assets:				
Money market funds [1]	$ 21,265	$ 21,265	$ —	$ —
Fixed income securities	26,906	—	26,906	—
Total	$ 48,171	$ 21,265	$ 26,906	$ —
Liabilities:				
Warrant liabilities	$ 13,128	$ —	$ —	$ 13,128
Total	$ 13,128	$ —	$ —	$ 13,128

(1) Money market funds are included within cash and cash equivalents in the accompanying consolidated balance sheets and are recognized at fair value.

The following table reflects the change in the Company's Level 3 liabilities, which consist of the warrants issued in a private placement in November 2016 (see Note 7), for the year ended December 31, 2018 (in thousands):

	November Private Placement Warrants
Balance at December 31, 2016	$ 6,333
Change in fair value	6,795
Balance at December 31, 2017	$ 13,128
Change in fair value	(4,617)
Balance at December 31, 2018	$ 8,511

6. ACCRUED EXPENSES AND OTHER CURRENT LIABILITIES

Accrued expenses as of December 31, 2018 and 2017 consisted of the following (in thousands):

	December 31, 2018	December 31, 2017
Clinical	$ 941	$ 1,093
Compensation and benefits	830	1,024
Accounting and legal	227	453
Other	369	164
Total accrued expenses and other current liabilities	$ 2,367	$ 2,734

7. STOCKHOLDERS' EQUITY

Common Stock

In June 2017, the Company issued and sold in an underwritten public offering an aggregate of 3,269,219 shares of its common stock at $13.00 per share, which included 384,604 shares pursuant to the exercise of an option to purchase additional shares granted to the underwriters in connection with the offering. The offering resulted in $39.7 million of net proceeds to the Company, after deducting underwriting discounts and commissions and other offering expenses payable by the Company.

In August 2017, the Company entered into a Controlled Equity Offering℠ Sales Agreement (the "Sales Agreement") with Cantor Fitzgerald & Co. ("Cantor"), pursuant to which the Company may offer and sell, from time to time through Cantor, shares of the Company's common stock having an aggregate offering price of up to $50.0 million. The Company will pay Cantor a commission rate equal to 3.0% of the aggregate gross proceeds from each sale. During the year ended December 31, 2018, the Company sold an aggregate of 217,329 shares of its common stock pursuant to the Sales Agreement at a weighted-average selling price of $15.42 per share, which resulted in $3.2 million of net proceeds to the Company. During the year ended December 31, 2017, the Company sold an aggregate of 252,443 shares of its common stock pursuant to the Sales Agreement at a weighted-average selling price of $15.55 per share, which resulted in $3.7 million of net proceeds to the Company.

In August 2018, the Company issued and sold in an underwritten public offering an aggregate of 3,246,079 shares of our common stock at $12.50 per share, which included 246,079 shares pursuant to the exercise of an option to purchase additional shares granted to the underwriters in connection with the offering. The offering resulted in $38.0 million of net proceeds, after deducting underwriting discounts and commissions and other offering expenses payable by the Company.

Warrants

In connection with the amendment and restatement of a license agreement with BioHEP in February 2016, the Company issued a warrant to purchase 125,000 shares of the Company's common stock to BioHEP (the "BioHEP Warrant"). The BioHEP Warrant had an exercise price of $16.00 per share. The Company evaluated the terms of the warrant and concluded that it should be equity-classified. The fair value of the warrant, $0.8 million, was estimated on the issuance date using a Black-Scholes pricing model based on the following assumptions: an expected term of two and a half years, expected stock price volatility of 71%, a risk-free rate of 1.01%, and a dividend yield of 0%. The fair value was expensed as research and development costs. The warrant expired unexercised on August 1, 2018.

In connection with the Company's IPO, the Company issued to the sole book-running manager for the IPO a warrant to purchase 27,600 shares of common stock in May 2016 and a warrant to purchase 747 shares of common stock in June 2016 (together, the "IPO Warrants"). The IPO Warrants are exercisable at an exercise price of $15.00 per share and expire on May 5, 2021. The Company evaluated the terms of the IPO Warrants and concluded that they should be equity-classified. The fair value of the May 2016 IPO Warrants was estimated on the applicable issuance dates using a Black Scholes pricing model based on the following assumptions: an expected term of 4.99 years; expected stock price volatility of 87%; a risk-free rate of 1.20%; and a dividend yield of 0%. The fair value of the June 2016 IPO Warrants was estimated on the applicable issuance dates using a Black Scholes pricing model based on the following assumptions: an expected term of 4.92 years; expected stock price volatility of 87%; a risk-free rate of 1.23%; and a dividend yield of 0%. The aggregate fair value of the IPO Warrants was $0.2 million.

In November 2016, the Company entered into a definitive agreement with respect to the private placement of 1,644,737 shares of common stock and warrants to purchase 1,644,737 shares of common stock (the "November 2016 Private Placement Warrants") to a group of accredited investors. These investors paid $9.12 for each share of common stock and warrant to purchase one share of common stock. The November 2016 Private Placement Warrants are exercisable at an exercise price of $10.79 per share and expire on November 23, 2021. The Company evaluated the terms of these warrants and concluded that they are liability-classified. In November 2016, the Company recorded the fair value of these warrants of approximately $8.3 million using a Black-Scholes pricing model. The Company must recognize any change in the value of the warrant liability each reporting period in the statement of operations. As of December 31, 2018 and 2017, the fair value of the November 2016 Private Placement Warrants was approximately $8.5 million and $13.1 million, respectively (see Note 5).

A summary of the Black Scholes pricing model assumptions used to record the fair value of the warrants is as follows:

	December 31, 2018	December 31, 2017
Risk-free interest rate	2.5%	2.0%
Expected term (in years)	2.9	3.9
Expected volatility	78.1%	73.1%
Expected dividend yield	0%	0%

The following table summarizes the warrant activity for the years ended December 31, 2018 and 2017 is as follows:

	Warrants
Outstanding at December 31, 2016	1,798,084
Grants	—
Exercises	(10,960)
Expirations/cancellations	—
Outstanding at December 31, 2017	1,787,124
Grants	—
Exercises	—
Expirations/cancellations	(125,000)
Outstanding at December 31, 2018	1,662,124

2014 Stock Incentive Plan

In April 2014, the Company's Board of Directors approved the 2014 Stock Incentive Plan (the "2014 Plan") and authorized 750,000 shares of common stock to be issued under the 2014 Plan. The Company's 2014 Plan provides for the issuance of common stock, stock options and other stock-based awards to employees, officers, directors, consultants, and advisors. The Company's 2015 Stock Incentive Plan (the "2015 Plan") became effective immediately prior to the closing of the Company's IPO on May 11, 2016. Upon the effectiveness of the 2015 Plan, 116,863 shares of common stock that remained available for grant under the 2014 Plan became available for grant under the 2015 Plan, and no further awards were available to be issued under the 2014 Plan.

2015 Stock Incentive Plan

The Board initially adopted the 2015 Plan in December 2015, subject to stockholder approval. The 2015 Plan become effective upon the closing of the Company's IPO on May 11, 2016 after approval by the Company's stockholders. The 2015 Plan provides for the issuance of common stock, stock options and other stock-based awards to employees, officers, directors, consultants and advisors of the Company.

In June 2018, upon receipt of stockholder approval at the Company's 2018 annual meeting, the 2015 Plan was amended and restated in its entirety increasing the authorized number of shares of common stock reserved for issuance by 800,000 shares (together with the 2014 Plan, the 2015 Plan, the "Stock Incentive Plans"). The Board approved the Amended and Restated 2015 Plan on March 9, 2018. Pursuant to the Amended and Restated 2015 Plan, there are 1,666,863 shares authorized for issuance. In addition, to the extent any outstanding awards under the 2014 Plan expire, terminate or are otherwise surrendered, cancelled or forfeited after the closing of the Company's IPO, those shares shall be added to the authorized shares under the Amended and Restated 2015 Plan. The total amount of shares authorized for issuance under both the 2014 Plan and the Amended and Restated 2015 Plan is 2,300,000. As of December 31, 2018, the Company had 939,322 shares available for issuance under the Amended and Restated 2015 Plan.

The exercise price of stock options cannot be less than the fair value of the common stock on the date of grant. Stock options awarded under the Stock Incentive Plans expire 10 years after the grant date, unless the Board sets a shorter term.

The following table summarizes the option activity under the Stock Incentive Plans for the years ended December 31, 2018 and 2017:

	Options	Weighted-Average Exercise Price Per Share	Aggregate Intrinsic Value
Options outstanding at December 31, 2016	704,315	$ 11.82	$ —
Granted	297,500	8.45	—
Exercised	(10,000)	9.28	11,228
Cancelled	(3,250)	12.44	—
Options outstanding at December 31, 2017	988,565	$ 10.83	$ 2,617,859
Granted	311,000	12.28	—
Exercised	—	—	—
Cancelled	—	—	—
Options outstanding at December 31, 2018	1,299,565	$ 11.18	$ 881,385
Options exercisable at December 31, 2018	748,511	$ 11.23	$ 499,147

As of December 31, 2018, all options outstanding have a weighted-average remaining contractual life of 7.6 years. The weighted-average fair value of all stock options granted for the year ended December 31, 2018 was $8.67. The intrinsic value at December 31, 2018 and 2017 is based on the closing price of the Company's common stock on that date of $10.39 per share and $13.44 per share, respectively.

In January 2018, the Company issued a stock option award as an inducement grant ("Inducement Award") for the purchase of an aggregate of 50,000 shares of the Company's common stock, outside of the Stock Incentive Plans, at an exercise price of $12.02 per share. The inducement grant is excluded from the option activity table above.

There were no stock options granted prior to 2015. The assumptions the Company used to determine the fair value of stock options granted in 2018 and 2017 are as follows, presented on a weighted-average basis:

	Year Ended December 31, 2018	2017
Risk-free interest rate	2.5%	2.0%
Expected term (in years)	5.9	6.0
Expected volatility	82.5%	80%
Expected dividend yield	0%	0%

The following table summarizes the stock-based compensation expense for the years ended December 31, 2018 and 2017 (in thousands):

	Year Ended December 31, 2018	2017
Stock-based compensation:		
Research and development	$ 843	$ 489
General and administrative	1,933	1,422
Total Stock-based compensation	$ 2,776	$ 1,911

The fair value of stock options vested during the year ended December 31, 2018 was $2.3 million. At December 31, 2018, there was $3.7 million of unrecognized stock-based compensation expense relating to stock options granted pursuant to the Plans, which will be recognized over the weighted-average remaining vesting period of 2.1 years.

Reserved Shares

As of December 31, 2018 and 2017, the Company reserved the following shares of common stock for issuance of shares resulting from the exercise of outstanding warrants and options, as well as the issuance of shares available for grant under the Stock Incentive Plans:

	December 31,	
	2018	2017
2016 BioHEP warrants	—	125,000
2016 IPO warrants	28,347	28,347
November Private Placement Warrants	1,633,777	1,633,777
2014 and 2015 Stock Incentive Plans	2,238,887	1,448,100
Inducement Award	50,000	—
Total	3,951,011	3,235,224

8. INCOME TAXES

In general, the Company has not recorded a provision for federal or state income taxes as it has had cumulative net operating losses since inception

On December 22, 2017 the President signed the Tax Cuts and Jobs Act (the "JOBS Act") which reduced the US corporate income tax rate to 21% effective January 1, 2018 as well as a variety of other changes including the limitation of the tax deductibility of interest expense, acceleration of expensing of certain business assets and reductions in the amount of executive pay that could qualify as a tax deduction. ASC 740 requires us to recognize the effect of the tax law changes in the period of enactment. The Company recalculated its deferred tax balances at the new 21% corporate tax rate and recorded an offset for the net amount as a component of income tax expense. This change was offset by a corresponding change in the valuation allowance because the Company maintains a full valuation allowance as of December 31, 2017. On December 22, 2017, the SEC staff issued Staff Accounting Bulletin ("SAB") 118, Income Tax Accounting Implications of the Tax Cuts and Jobs Act ("SAB 118"), which provides guidance on accounting for the impact of the JOBS Act, in effect allowing an entity to use a methodology similar to the measurement period in a business combination. Pursuant to the disclosure provisions of SAB 118, as of December 31, 2017 the Company made a reasonable estimate of the effects of the JOBS Act on its existing deferred tax balances. The Company completed its accounting for the tax effects of the JOBS Act as of December 31, 2018 and did not record any material adjustments to the original estimate.

A reconciliation of the statutory U.S. Federal Tax Rate to the Company's effective tax rate is as follows:

	Year Ended December 31,	
	2018	2017
U.S. statutory federal income tax rate	(21.0)%	(34.0)%
State income taxes, net of federal income tax benefit	(7.6)%	(3.8)%
Permanent items	0.6%	0.8%
Warrant adjustment	(4.2)%	8.3%
R&D credit	(0.6)%	(0.3)%
Change in valuation allowance	32.7%	—
Change in federal rate impact	—	29.2%
Other	0.1%	(0.2)%
Effective income tax rate	0.0%	0.0%

The significant components of the Company's deferred tax assets as of December 31, 2018 and 2017 are as follows (in thousands):

	December 31, 2018	2017
Net operating loss carryforwards	$ 23,582	$ 16,781
Research and development credits	649	520
Accrued expenses	209	265
Property and equipment	(37)	(11)
License payments	612	663
Stock based compensation	1,383	831
Other – net	138	22
Deferred tax assets	26,536	19,071
Valuation allowance	(26,536)	(19,071)
Net deferred tax asset and liability	$ —	$ —

Because of the Company's recurring losses since inception, management has concluded that it is more likely than not that the benefits of losses to date which result in deferred tax assets will not be realized and, accordingly, the Company provided a full valuation allowance against the net deferred tax assets. The valuation allowance increased by approximately $7.5 million in 2018 due to the increase in the deferred tax assets (primarily due to the net operating loss carryforwards). In comparison, the valuation allowance increased by approximately $8,000 in 2017 due to the increase in the deferred tax assets (primarily due to the net operating loss carryforwards) largely offset by a decrease from the deferred tax assets previously being valued at 34% and now being valued at 21%. At December 31, 2018, the Company had federal and state net operating loss carryforwards of approximately $86.3 million and $86.4 million, respectively, available to reduce future taxable income, if any. The federal net operating loss carryforwards expire beginning in 2029 and ending in 2037, with the exception of federal net operating losses created after tax years ending December 31, 2017. These net operating loss carryforwards have an indefinite life and do not expire. The state net operating loss carryforwards expire beginning in 2029 and ending in 2038 At December 31, 2018, the Company had available federal and state income tax credits of approximately $294,000 and $449,000, respectively, which are available to reduce future income taxes, if any, through 2038.

Realization of the future tax benefits is dependent on many factors, including the Company's ability to generate taxable income within the net operating loss carryforward period. Under the provisions of the Internal Revenue Code, the net operating loss and tax credit carry-forwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating loss and tax credit carry-forwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitations is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has completed several financings since its inception, which may have resulted in a change in control as defined by Sections 382 and 383 of the Internal Revenue Code, or could result in a change in control in the future. The Company has performed a Section 382 study from its inception through December 31, 2017. The Company determined it experienced two ownership changes, but it expects to be able to utilize all its tax attributes despite the limitations calculated from the ownership changes. If ownership changes occur in the future, they could limit the amount of tax attributes available to offset tax due and increase the Company's tax expense adversely. The Company will continue to monitor changes in its ownership and update its Section 382 study in the future for those changes before its tax attributes are utilized.

The Company has generated research and development tax credits but has not conducted a study to document its activities that qualify for research and development tax credits. This study may result in an adjustment to the Company's research and development credit carryforwards; however, since the Company has not conducted a study any adjustment is unknown, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development tax credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the deferred tax asset established for the research and development tax credit carry-forwards and the valuation allowance.

The Company files income tax returns in the U.S. federal and Massachusetts jurisdictions. The statute of limitations for assessment by the Internal Revenue Service, or IRS, and state tax authorities is closed for tax years prior to 2015, although carryforward attributes that were generated prior to tax year 2015 may still be adjusted upon examination by the IRS or state tax authorities if they either have been or will be used in a future period. The Company is currently not under examination by the Internal Revenue Service or any other jurisdictions for any tax years. The Company's policy is to record interest and penalties on any unrecognized tax benefits as part of tax expense. The Company has not recorded any interest or penalties on any unrecognized tax benefits since its inception. The Company does not believe material uncertain tax positions have arisen to date.

During the first quarter of 2016, the FASB issued ASU 2016-09 that amends its guidance on certain aspects of accounting for share-based payments to employees. Companies will no longer record excess tax benefits and tax deficiencies related to stock compensation in addition paid-in capital (APIC). Excess tax benefits occur when the amount deductible for an award of equity instruments on the employer's tax return is more than the cumulative compensation cost recognized for financial reporting purposes. Tax deficiencies occur when the amount deductible for an award of equity instruments on the employer's tax return is less than the cumulative compensation cost recognized for financial reporting purposes. Under ASU 2016-09, all excess tax benefits and tax deficiencies are recorded as income tax expense or benefit in the income statement in the interim period in which they occur. The Company adopted ASU 2016-09 in the first quarter of 2017 and there was no impact to the income tax provision or footnote as a result of the adoption because the Company did not have any historical excess tax benefits.

9. COMMITMENTS AND CONTINGENCIES

Leases

In March 2016, the Company entered into an operating lease for its former headquarters in Hopkinton, Massachusetts with a lease term through May 31, 2021. The total payments due during the term of the lease are approximately $771,000. The Company vacated the premises as of June 1, 2018 and in July 2018, the Company entered into a sublease agreement to sublease its former Hopkinton, Massachusetts premises. The Company incurred a loss on the lease of approximately $269,000, net of expected sublease income of approximately $294,000. The loss on the lease is included the general and administrative expenses in the consolidated statement of operations and in other current liabilities (for the short-term liability) and other long-term liabilities (for the remaining long-term liability) in the consolidated balance sheet.

In October 2017, the Company entered into a lease agreement for the Company's new principal office and laboratory space located in Hopkinton, Massachusetts. The initial term of the lease is 125 months beginning on June 1, 2018, the date the Company began occupying the new premises. The Company has the option to extend the lease one time for an additional 5-year period. Following an eleven-month rent abatement period, the Company will be obligated to make monthly rent payments in the amount of $34,699, which is subject to increase by approximately 3% annually for the first five years of the lease and by approximately 2.5% annually thereafter. The total lease payments due during the term of the lease are approximately $4.4 million. In addition, the Company is responsible under the lease for specified costs and charges, including certain operating expenses, utilities, taxes and insurance.

Rent paid under both leases for the years ended December 31, 2018 and 2017 was $207,000 and $233,000, respectively.

Future minimum commitments due under all leases at December 31, 2018 are as follows (in thousands):

Year		
2019	$	417
2020		588
2021		508
2022		450
Thereafter		2,867
Total minimum lease payments	$	4,830

The commitments under the lease agreement entered into in October 2017 are included in the table above.

BioHEP Technologies Ltd. License Agreement

In January 2016, the Company entered into an amended and restated license agreement with BioHEP, which became effective on February 1, 2016.

Under the amended and restated license agreement, the Company agreed to pay BioHEP up to $3.5 million in development and regulatory milestone payments for disease(s) caused by each distinct virus for which the Company develops licensed product(s). BioHEP is also eligible to receive tiered royalties in the low-to-mid single-digits on net product sales of licensed products by the Company and its affiliates and sub licensees, and a specified share of non-royalty sublicensing revenues the Company and its affiliates receive from sub licensees, which share of sublicensing revenues is capped at a maximum aggregate of $2.0 million under all such sublicenses. Milestone and royalty payments associated with the Company's amended and restated license agreement with BioHEP have not been included in the above table of contractual obligations as the Company cannot reasonably estimate if or when they will occur. As of December 31, 2018, there have been no milestone or royalty payments made to BioHEP.

Contingencies

The Company accrues for contingent liabilities to the extent that the liability is probable and estimable. There are no accruals for contingent liabilities in these consolidated financial statements.

10. 401(k) PLAN

The Company has a 401(k)-defined contribution plan (the "401(k) Plan") for substantially all of its employees. Eligible employees may make pretax contributions to the 401(k) Plan up to statutory limits. At the election of its Board, the Company may elect to match employee contributions. For the years ended December 31, 2018 and 2017, the Company paid a match of up to 4%, up to the maximum permitted by the Internal Revenue Code, which amounted to $142,000 and $124,000, respectively.

11. RELATED PARTY TRANSACTIONS

During the years ended December 31, 2018 and 2017, the Company had no material related party transactions.

12. SUBSEQUENT EVENTS

The Company has evaluated subsequent events through the date on which the consolidated financial statements were issued, to ensure that this submission includes appropriate disclosure of events both recognized in the consolidated financial statements and events which occurred subsequently but were not recognized in the consolidated financial statements.

Management

Martin Driscoll has been our President, Chief Executive Officer and Director since August 2015.

R. P. "Kris" Iyer, Ph.D. is one of our founders and has been our Chief Scientific Officer and a member of our board of directors since our inception in 2002.

Nezam H. Afdhal, M.D. has been our Chief Medical Officer since November 2015 and served as a consultant to us from early 2011 to November 2015.

Jonathan Freve, CPA, has been our Chief Financial Officer and Treasurer since January 2015.

Non-Employee Directors

Scott Smith has been a member of our Board of Directors since August 2018 and was appointed as chairman of our Board of Directors effective January 1, 2019. Mr. Smith currently serves as the President of Bioalta, LLC, a privately held biotechnology company.

David Arkowitz has been a member of our Board of Directors since January 2014. Mr. Arkowitz currently serves as the Chief Financial Officer and Treasurer of Flexion Therapeutics, Inc., a publicly traded biotechnology company.

Todd Brady, M.D., Ph.D., has been a member of our Board of Directors since July 2016. Dr. Brady currently serves as Chief Executive Officer and President of Aldeyra Therapeutics, Inc., a publicly traded biotechnology company.

Timothy Clackson, Ph.D. has been a member of our Board of Directors since March 2018. Dr. Clackson currently serves as President and Executive Vice President of Research and Development of Akrevia Therapeutics, a privately held biotechnology company.

Kurt Eichler has been a member of our Board of Directors since July 2015. Since his retirement from LCOR, Inc. in October 2013, Mr. Eichler has been self-employed in several real estate related investment and development ventures.

Accounting Firm

RSM US LLP
80 City Square
Boston, MA 02129

Transfer Agent

Computershare Trust Company
250 Royall Street
Canton, MA 02021

Forward-Looking Statements

Any statements in this 2018 annual report about our future expectations, plans and prospects, including statements regarding our strategy, future operations, prospects, plans and objectives, and other statements containing the words "believes," "anticipates," "plans," "expects," "potential," "could," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: whether our cash resources will be sufficient to fund our continuing operations for the period anticipated; whether results obtained in preclinical studies and early clinical trials will be indicative of results obtained in future clinical trials; whether any product candidates will advance through the clinical trial process on a timely basis and receive approval from the United States Food and Drug Administration or equivalent foreign regulatory agencies; whether, if any product candidate obtains approval, it will be successfully distributed and marketed; and other factors discussed in the "Risk Factors" section of our Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 11, 2019. In addition, the forward-looking statements included in this 2018 annual report represent our views as of May 24, 2019. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we specifically disclaim any obligation to do so.

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