

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

FORM 10-K

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 001-38697

PhaseBio Pharmaceuticals, Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

03-0375697
(I.R.S. Employer
Identification No.)

1 Great Valley Parkway, Suite 30
Malvern, Pennsylvania 19355
(Address including zip code of principal executive offices)

(610) 981-6500
(Registrant's telephone number, including area code)

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

(Title of Class)	(Name of exchange on which registered)
Common Stock, par value \$0.001 per share	The Nasdaq Stock Market, LLC

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

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the 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, smaller reporting company, or an 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	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
		Emerging growth company	<input checked="" type="checkbox"/>

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 registrant was not a public company as of the last business day of its most recently completed second fiscal quarter and therefore, cannot calculate the aggregate market value of its voting and non-voting common equity held by non-affiliates as of such date.

Class of Common Stock	Outstanding Shares as of March 15, 2019
Common Stock, \$0.001 par value	24,498,425

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement, to be filed pursuant to Regulation 14A under the Securities Exchange Act of 1934, for its 2019 Annual Meeting of Stockholders are incorporated by reference in Part III of this Form 10-K.

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SPECIAL CAUTIONARY NOTICE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or this Annual Report, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, that involve substantial risks and uncertainties. The forward-looking statements are contained principally in Part I, Item 1. “Business,” Part I, Item 1A. “Risk Factors,” and Part II, Item 7. “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” but are also contained elsewhere in this Annual Report. In some cases, you can identify forward-looking statements by the words “may,” “might,” “will,” “could,” “would,” “should,” “expect,” “intend,” “plan,” “objective,” “anticipate,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue” and “ongoing,” 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, levels of activity, 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, we caution you that these 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 timing, progress and results of clinical trials of PB2452, PB1046 and any other product candidates, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available and our research and development programs;
- the timing of any submission of filings for regulatory approval of PB2452, PB1046 and any other product candidates and our ability to obtain and maintain regulatory approvals for PB2452 and PB1046 for any indication;
- our expectations regarding the size of the patient populations, market acceptance and opportunity for and clinical utility of our product candidates, if approved for commercial use;
- our manufacturing capabilities and strategy, including the scalability and commercial viability of our manufacturing methods and processes and our ability to maintain agreements with third parties;
- our expectations regarding the scope of any approved indication for PB2452 and PB1046;
- our ability to successfully commercialize our product candidates;
- our ability to leverage our proprietary elastin-like polypeptide technology to identify and develop future product candidates
- our estimates of our expenses, ongoing losses, future revenue, capital requirements and our needs for or ability to obtain additional financing;
- our ability to establish or maintain collaborations or strategic relationships;
- our ability to identify, recruit and retain key personnel;
- our ability to protect and enforce our intellectual property position for our product candidates, and the scope of such protection;
- our financial performance;

- our competitive position and the development of and projections relating to our competitors or our industry;
- the impact of laws and regulations; and
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act.

You should refer to “Item 1A. Risk Factors” in this Annual Report 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 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, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. The forward-looking statements in this Annual Report represent our views as of the date of this Annual Report. We anticipate that subsequent events and developments may cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, 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. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Annual Report.

You should read this report and the documents that we reference in this report, completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

All brand names or trademarks appearing in this Annual Report are the property of their respective owners. Solely for convenience, the trademarks and trade names in this Annual Report are referred to without the symbols ® and ™, but such references should not be construed as any indication that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. Unless the context requires otherwise, references in this report to “PhaseBio,” the “Company,” “we,” “us,” and “our” refer to PhaseBio Pharmaceuticals, Inc.

Item 1. Business.

Overview

We are a clinical-stage biopharmaceutical company focused on the development and commercialization of novel therapies to treat orphan diseases, with an initial focus on cardiopulmonary indications. Our lead product candidate, PB2452, is a novel reversal agent for the antiplatelet drug ticagrelor, which we are developing for the treatment of patients on ticagrelor who are experiencing a major bleeding event or those who require urgent surgery. We recently completed a Phase 1 clinical trial of PB2452 in healthy subjects and intend to initiate a Phase 2a clinical trial in healthy older subjects in the first half of 2019. Our second product candidate, PB1046, is a once-weekly fusion protein currently in a Phase 2b clinical trial for the treatment of pulmonary arterial hypertension, or PAH. PB1046 utilizes our proprietary half-life extending elastin-like polypeptide, or ELP, technology, which also serves as the engine for our preclinical pipeline. We retain worldwide rights to all of our product candidates.

PB2452 is a novel recombinant human monoclonal antibody antigen-binding fragment, or Fab fragment, designed to reverse the antiplatelet activity of ticagrelor. Ticagrelor is an antiplatelet therapy widely prescribed to reduce the rates of death, heart attack and stroke in patients with acute coronary syndrome, or ACS, or who have previously experienced a heart attack. The American College of Cardiology, American Heart Association and European Society of Cardiology guidelines recognize ticagrelor as the preferred antiplatelet therapy for ACS. In 2018, ticagrelor, currently marketed by AstraZeneca plc, or AstraZeneca, under the brand names Brilinta and Brilique, had worldwide sales of \$1.3 billion, an increase of 22% over 2017 sales. In the fourth quarter of 2018, ticagrelor had worldwide sales of \$376 million, an increase of 26% over sales in the fourth quarter of 2017. Ticagrelor binds to platelets to prevent them from forming blood clots, which could restrict blood flow to critical organs in these patients, causing heart attacks or strokes. Due to ticagrelor's antiplatelet activity, patients on ticagrelor have an elevated risk of spontaneous bleeding. In addition, patients on ticagrelor who need urgent surgery cannot wait the recommended five days for ticagrelor's effect to dissipate and are at increased risk of major bleeding during and after surgery. There are currently no known reversal agents approved or in clinical development for ticagrelor or any of the other antiplatelet drugs. In our Phase 1 clinical trial, PB2452 achieved immediate and complete reversal of ticagrelor's antiplatelet activity, with potential customizable duration of reversal based on the dosing regimen, which we believe has the potential to bring life-saving therapeutic benefit to these patients by increasing the safety of ticagrelor. We believe the availability of a reversal agent could expand ticagrelor's use by mitigating concerns regarding bleeding risk and uniquely position ticagrelor as the only oral antiplatelet drug with a reversal agent.

We recently completed a Phase 1 dose escalation clinical trial of PB2452 in healthy subjects ages 18 to 50 who had been pre-dosed with ticagrelor. In this trial, we observed immediate and complete reversal of ticagrelor's antiplatelet activity within five minutes following initiation of infusion, and sustained reversal for over 20 hours in later dosing cohorts in which we administered PB2452 over an extended infusion period.

Based on our observations in our Phase 1 trial, duration of reversal may be controlled by duration of the infusion, which may allow for customization based on patient needs. There were no PB2452-related adverse events, or AEs, or serious adverse events, or SAEs, in any of the dose cohorts. We believe that the results of the Phase 1 trial support the continued development of PB2452 to treat ticagrelor patients who are experiencing a major bleeding event or those who require urgent surgery.

We intend to initiate a Phase 2a clinical trial of PB2452 in healthy older subjects in the first half of 2019 in order to evaluate safety and efficacy of the potentially therapeutic doses and dosing regimens from the Phase 1 trial in this population. Older adults exhibit more variability in drug response to ticagrelor and higher levels of baseline platelet reactivity compared to younger subjects, and they resemble the patient population most likely to be treated with ticagrelor and potentially benefit from PB2452, if approved. We intend to design the Phase 2a trial to identify the most appropriate dose and dosing regimen of PB2452 for our planned Phase 2b and Phase 3 clinical trials.

In mid-2019, we intend to request a meeting with the U.S. Food and Drug Administration, or the FDA, to review the clinical profile of and confirm the regulatory pathway for PB2452. Subject to discussions with the FDA, we intend to initiate a multi-center Phase 2b clinical trial of PB2452 in healthy older adults in the second half of 2019. Subject to discussions with the FDA, we intend to initiate a multi-center phase 2b clinical trial of PB2452 in healthy older subjects in the second half of 2019 and an international, multi-center phase 3 clinical trial in patients on ticagrelor who are experiencing a major bleeding event or require urgent surgery in 2020. The FDA's accelerated approval regulations allow drugs that are being developed to treat an unmet medical need for serious conditions to be approved substantially based on evidence of an effect on a surrogate biomarker endpoint that is considered reasonably likely to predict clinical benefit, rather than a clinical endpoint such as survival or irreversible morbidity. If considered appropriate by the FDA, we intend to pursue accelerated approval, which would allow us to submit a biologics license application, or BLA, prior to completion of the Phase 3 clinical trial based on biomarker data from an initial subset of the Phase 3 patients. If we were to receive accelerated approval, the completion of the Phase 3 trial would be a post-marketing commitment.

PB1046 is being developed as a once-weekly, novel treatment for PAH, a progressive, life-threatening, orphan disease caused by vasoconstriction and structural deterioration of the pulmonary arteries, which can lead to heart failure and, eventually, death. PB1046 is a subcutaneously-injected, sustained release analogue of the native human peptide vasoactive intestinal peptide, or VIP. VIP is a neurohormone that relaxes the muscles surrounding blood vessels, causing them to dilate, which results in improved blood flow. In contrast to the currently approved therapies for PAH, which only target vasodilation, we believe that VIP also suppresses the adverse remodeling of blood vessels and increases cardiac contractility and relaxation. We believe that PB1046 has the potential to be disease-modifying and complementary to current standard of care therapies for PAH.

We have completed two clinical trials of subcutaneously-injected PB1046 in subjects with cardiovascular diseases. In these trials, PB1046 was observed to be well tolerated, with no drug-related SAEs. In both trials, we observed that patients who received PB1046 experienced statistically significant reductions in blood pressure that were sustained for at least one week, with no reported episodes of symptomatic hypotension. We have also completed enrollment of an exploratory Phase 1b/2a clinical trial to evaluate the effects of PB1046 on pulmonary arterial pressure in PAH patients with a CardioMEMS device, an implanted hemodynamic monitor that continuously reports pulmonary arterial pressure and cardiac function. In preliminary results from this trial, we have observed reductions in pulmonary arterial pressure and increases in cardiac output, which we believe are consistent with potential beneficial effects of PB1046. We have begun dosing patients in a randomized, double-blinded, controlled Phase 2b clinical trial in approximately 60 PAH patients to assess the safety, tolerability and efficacy of PB1046. This clinical trial will evaluate the effects of PB1046 on pulmonary arterial pressure and exercise tolerance, including the distance the patient can walk in six minutes, which is an important clinical endpoint that the FDA has previously used as the basis for approval of other PAH drugs. We expect to report results from this trial in 2020.

PB1046 and our preclinical product candidates are based on our proprietary ELP technology. Our ELP technology extends the circulating half-life of proteins and peptides and also provides a sustained-release mechanism, resulting in exposure of active molecules for periods of a week or longer from a single subcutaneous injection. We believe that our ELP technology enhances solubility, stability and bioavailability, provides extended drug exposure and creates product candidates that are straightforward to manufacture and administer. Our strategy is to apply our ELP technology to proteins and peptides with well-characterized therapeutic activities but suboptimal half-lives to improve their pharmacokinetics, enable their use as pharmaceutical products and allow for more convenient dosing regimens. To date, we have not observed any drug-related SAEs in any of the over 500 subjects in clinical trials of our ELP product candidates.

We have an experienced management team that includes individuals with experience in translational research, orphan and cardiopulmonary drug discovery, development and commercialization. We are led by our Chief Executive Officer, Jonathan P. Mow, who brings more than 25 years of experience in biotechnology management, including previous executive experience at Amylin Pharmaceuticals, Corus Pharma, PathoGenesis and Bristol-Myers Squibb.

Strategy

Our strategy is to identify, develop and commercialize therapies to treat orphan diseases, with an initial focus on cardiopulmonary indications. The key elements of our strategy include:

- **Continue to advance PB2452 through clinical development and regulatory approval.** We intend to develop and commercialize PB2452 as a novel reversal agent for the antiplatelet drug ticagrelor. We recently completed a Phase 1 dose escalation clinical trial of PB2452, delivered as an intravenous infusion, in healthy subjects that was designed to identify the dose and dosing regimen, determine proof of concept and evaluate the safety and tolerability of PB2452. We intend to initiate a Phase 2a clinical trial of PB2452 in healthy older subjects in the first half of 2019 in order to evaluate safety and efficacy of the potential therapeutic doses and dosing regimens from the Phase 1 trial in this population. Subject to discussions with the FDA, we intend to initiate a multi-center Phase 2b clinical trial in healthy older adults in the second half of 2019. Based on a planned interim assessment of an initial subset of patients in this trial, we plan to initiate an international, multi-center Phase 3 clinical trial in patients on ticagrelor who are experiencing a major bleeding event or require urgent surgery. If considered appropriate by the FDA, we intend to pursue accelerated approval, which would allow us to submit a BLA prior to completion of the Phase 3 clinical trial based on biomarker data from an initial subset of the Phase 3 patients.
- **Continue to develop PB1046.** We intend to advance PB1046 through clinical trials as a once-weekly novel treatment for PAH that is vasodilatory, potentially disease-modifying and complementary to the current standard of care therapies. We are currently conducting a Phase 2b clinical trial of PB1046 and expect to report results from this trial in 2020. Based on the results of this trial, we intend to advance this product candidate into Phase 3 clinical development for the treatment of PAH.
- **Broaden the potential therapeutic applications of PB1046.** Due to improvements in pharmacokinetics that we have observed with our ELP technology, we believe that the therapeutic potential of VIP can be applied to a variety of other orphan indications. Preclinical data suggest PB1046 may have clinical benefit in cardiomyopathy associated with Duchenne Muscular Dystrophy, or DMD, heart failure and other cardiomyopathies and in cystic fibrosis. As such, we intend to strategically broaden the therapeutic applications of PB1046 by exploring its development in additional indications.
- **Leverage our ELP technology platform to expand our development pipeline.** We believe that our ELP technology enhances solubility, stability and bioavailability, provides extended drug exposure and creates product candidates that are straightforward to manufacture and administer. As such, we plan to utilize our platform to identify product candidates for additional orphan indications. We intend to apply our ELP technology to improve the pharmacokinetics of proteins and peptides with well-characterized therapeutic activities but suboptimal half-lives, in order to improve their pharmacokinetics, enable their use as pharmaceutical products and allow for more convenient dosing regimens.
- **Commercialize our product candidates.** We have entered into exclusive license agreements with AstraZeneca for PB2452 and Duke University for our ELP technology pursuant to which we retain worldwide commercial rights to our product candidates. If approved in the United States, we intend to commercialize PB2452 independently, and we may either commercialize PB1046 independently or in collaboration with a partner. As we advance towards regulatory approvals for our product candidates, we intend to establish a focused marketing and sales infrastructure. We may also explore collaborations or partnerships to commercialize PB2452 and PB1046 outside of the United States.

Pipeline

Our pre-clinical and clinical-stage pipeline is set forth below:

Program	Indication/Therapeutic Area	Pre-Clinical	Phase 1	Phase 2	Phase 3	WW Commercial Rights	Milestones
PB2452	Reversal of Ticagrelor Antiplatelet Activity	Phase 2 ongoing				PHASE	1H 2019: Initiate Phase 2a Report Phase 2a results 2H 2019: Initiate Phase 2b 2020: Initiate Phase 3 based on plan to pursue accelerated regulatory pathway
PB1046	Pulmonary Arterial Hypertension (PAH)	Phase 2 ongoing				PHASE	2020: Phase 2b results
GLP2-ELP	Short Bowel Syndrome	IND-enabling activities				PHASE	
CNP-ELP	Achondroplasia	Late research				PHASE	
Early Programs	PROPRIETARY LONG ACTING INJECTABLE RECOMBINANT BIOPOLYMERS (Elastin-like Polypeptides – ELPs)						

PB2452: Antiplatelet Therapy Reversal Agent for Ticagrelor

Our lead product candidate, PB2452, is a novel ticagrelor reversal agent, which we are developing for the treatment of patients on ticagrelor who are experiencing a major bleeding event or who require urgent surgery. We recently completed a Phase 1 dose escalation clinical trial of PB2452, delivered as an intravenous infusion, in healthy subjects that was designed to identify the dose and dosing regimen, determine proof of concept and evaluate the safety and tolerability of PB2452. We intend to initiate a Phase 2a clinical trial in healthy older subjects in the first half of 2019.

Background on Acute Coronary Syndrome

ACS describes a range of conditions associated with sudden reduced blood flow to the heart, including unstable angina and myocardial infarction, or heart attack. ACS is caused by the inappropriate formation of clots in the coronary arteries. These blood clots are made up primarily of platelets, small lens-shaped cells found in the blood that normally aggregate at sites of injury to help stop bleeding. According to the Centers for Disease Control and Prevention, approximately 790,000 Americans have a heart attack every year, and heart attacks are a leading cause of death in the developed world.

The primary treatment for ACS is the use of antiplatelet drugs to prevent the worsening of existing clots or to reduce the formation of additional clots. These clots can occur in the heart or in stents that are placed in the blocked coronary artery to keep the blood vessel open or elsewhere in the body. Without antiplatelet drugs, patients are at a significantly increased risk of recurrent heart attacks, stroke and death. The standard of care for ACS patients is dual antiplatelet therapy, or DAPT, which is a combination of aspirin and an inhibitor of a specific receptor found on platelets known as the P2Y₁₂ receptor. This combination is started after a patient experiences a heart attack or other manifestation of ACS and has been shown to significantly reduce platelet aggregation and clot formation and reduce the frequency of recurrent heart attacks, stroke and death.

While the antiplatelet drugs used in DAPT have proven effective at improving overall outcomes in ACS patients, their suppression of blood clotting increases patients' risk of bleeding. Bleeding events in patients on antiplatelet therapy, which can occur spontaneously or as a result of injury or surgery, are classified as minor or major. In the 18,000-patient clinical trial, Platelet Inhibition and Patient Outcomes, or PLATO, conducted by AstraZeneca, ticagrelor was shown to be superior to the antiplatelet drug clopidogrel, marketed under the brand name Plavix, in reducing recurrent heart attack, stroke and death in patients with ACS. However, in both treatment groups, 11% to 12% of patients in the trial suffered major bleeding events, and in 5.8% of patients, these major bleeding events were fatal or life-threatening. The causes of bleeding varied in the trial population. In approximately 3% of the patients on ticagrelor, the major bleeding events were spontaneous and not related to any medical

procedure, whereas approximately 9% of patients on ticagrelor developed major bleeding that was related to procedures like coronary artery bypass surgery, or CABG. Although the trial protocol recommended that patients who needed CABG stop taking ticagrelor for one to three days prior to surgery, nearly half of all ticagrelor patients needed surgery urgently and could not wait the up to three days for ticagrelor's effect to dissipate so normal blood clotting could be restored. Overall, up to 80% of patients who underwent CABG surgery in the trial suffered a major or life-threatening bleeding event related to the surgery, and for those who needed urgent surgery and could not wait three days for the effects of ticagrelor to dissipate, approximately 50% experienced a fatal or life-threatening bleeding event. While some of this risk was likely associated with patients' underlying conditions, the overall bleeding risk is significantly increased by antiplatelet drugs, and the current U.S. and European prescribing information for ticagrelor suggests suspension of ticagrelor treatment for five days and seven days, respectively, prior to surgery.

Despite the increased bleeding risk, antiplatelet drugs, along with anticoagulant drugs which are used to prevent clots in veins, represent some of the most widely prescribed drugs in the United States due to their lifesaving effects. While both of these classes of drugs increase the risk of bleeding, reversal agents have been developed for anticoagulant drugs, but to date, no reversal agents exist for antiplatelet drugs. In the absence of a reversal agent, physicians have limited treatment options, and sometimes administer platelet transfusions, which are unproven in this setting. The ability to quickly reverse the antiplatelet activity of ticagrelor and restore normal clotting would increase its safety, both in instances of major bleeding as well as in situations where surgical or other medical interventions associated with bleeding are urgently needed.

Background on Antiplatelet Drugs

The three oral antiplatelet P2Y₁₂ receptor antagonist drugs prescribed in DAPT are clopidogrel, marketed under the brand name Plavix, prasugrel, marketed under the brand name Effient, and ticagrelor, marketed under the brand names Brilinta and Brilique. Unlike clopidogrel and prasugrel that permanently bind to and inhibit the target receptors on platelets, ticagrelor binds to the P2Y₁₂ receptor in a transient manner, quickly cycling on and off the receptor. We believe this transient binding of ticagrelor presents a unique opportunity to develop a specific reversal agent for ticagrelor, whereas the permanent binding of the other drugs to the receptor precludes a reversal agent from being developed.

Ticagrelor is considered the best-in-class P2Y₁₂ antiplatelet agent because it has demonstrated superior efficacy compared to clopidogrel. In 2017, ticagrelor accounted for 17% of new P2Y₁₂ antiplatelet prescriptions in the United States. In 2018, ticagrelor had worldwide sales of \$1.3 billion, an increase of 22% over 2017 sales. Ticagrelor has achieved this level of market share despite the availability of generic versions of clopidogrel and prasugrel. We believe ticagrelor growth is being driven in part by treatment guidelines from the American College of Cardiology, American Heart Association and the European Society of Cardiology that recognize ticagrelor as the preferred antiplatelet treatment for ACS. We believe that the availability of a reversal agent could further drive the use of ticagrelor by making it the only reversible oral P2Y₁₂ antiplatelet treatment, thereby conferring a possible safety benefit over the other agents. Furthermore, based on the growth of clopidogrel prescriptions after the introduction of a generic form of that drug, we believe ticagrelor prescriptions could grow significantly after its patents expire and generic competition drives prices down to similar levels as other P2Y₁₂ antiplatelet therapies.

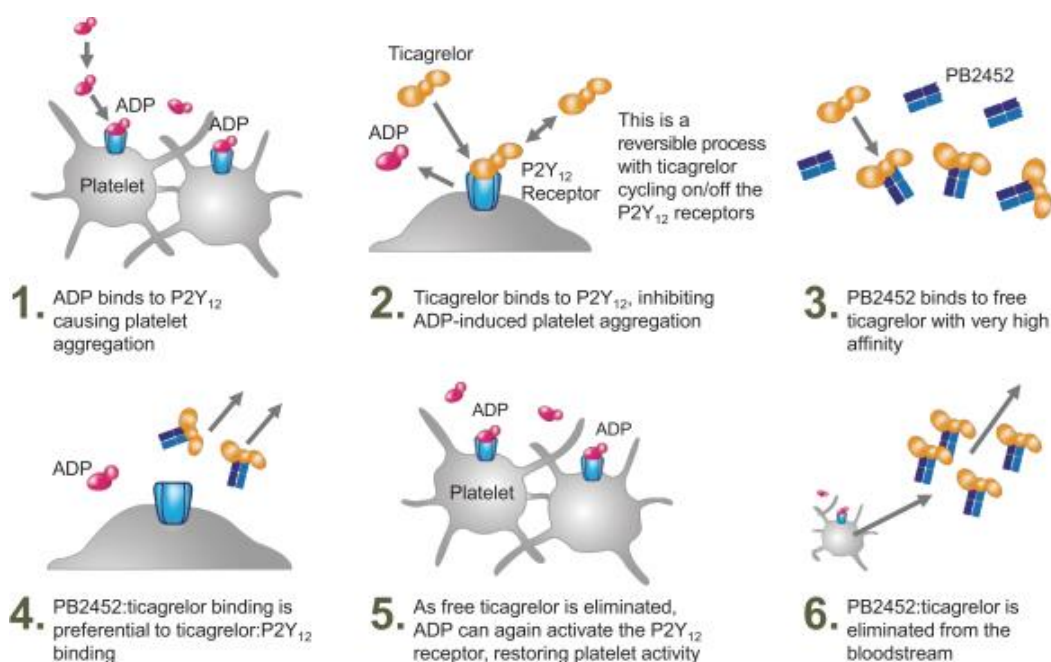
Our Solution: PB2452

PB2452 is a human Fab fragment that binds to ticagrelor with high affinity and specificity to reverse ticagrelor's antiplatelet activity. We believe that the availability of PB2452 may further differentiate ticagrelor from other P2Y₁₂ receptor antagonists by providing for better clinical management of the balance between the desired antiplatelet effect and prevention or control of bleeding. We exclusively licensed PB2452 from MedImmune Limited, or MedImmune, a wholly owned subsidiary of AstraZeneca.

PB2452 Background

Ticagrelor works by binding to the P2Y₁₂ receptor on platelets, thereby preventing adenosine diphosphate, or ADP, from causing platelet aggregation. Ticagrelor binds transiently to the P2Y₁₂ receptor quickly cycling on and off, allowing PB2452 to bind to free ticagrelor, thereby preventing ticagrelor's inactivation of the receptor and removing ticagrelor from circulation. With ticagrelor removed, ADP can once again activate the P2Y₁₂ receptor and induce platelet aggregation. This activity is illustrated below.

Mechanism of action of ticagrelor and its reversal by PB2452



PB2452 binds to ticagrelor with an affinity that is approximately 100 times stronger than ticagrelor's affinity for the P2Y₁₂ receptor. This high affinity enables PB2452 to bind to free ticagrelor, resulting in an immediate reversal of ticagrelor's effect and restoration of platelet activity.

Clinical Development of PB2452

Phase 1 Clinical Trial

We recently completed a Phase 1 dose escalation clinical trial of PB2452, delivered as an intravenous infusion, in healthy subjects pre-dosed with ticagrelor that was designed to identify the target dose, determine proof of concept and evaluate the safety and tolerability of PB2452. In the trial, we observed that PB2452 immediately and completely reversed the antiplatelet effects of ticagrelor. We conducted this trial pursuant to an investigational new drug, or IND, application that we sponsored and that became effective in March 2018. In March 2019, the full results from this trial of PB2452 were published in the *New England Journal of Medicine*.

Our Phase 1 clinical trial enrolled 64 subjects across 10 dose cohorts. Based on pharmacokinetic and pharmacodynamic data from the early dose cohorts in the trial, we adjusted the intravenous infusion of PB2452 to identify the optimal dose and dosing regimen for future trials and for the target patient populations. The initial three cohorts of subjects were dosed with 30-minute intravenous infusions of PB2452 alone in order to assess pharmacokinetics and safety. Subsequent cohorts were pre-dosed with the standard clinical regimen of ticagrelor for two days prior to administration of PB2452 to enable direct assessment of reversal of ticagrelor's inhibition of platelet aggregation using platelet function assays. There were no PB2452-related AEs or SAEs in any of the dose cohorts.

In cohorts 5 and 6, which were the first cohorts in which potentially pharmacodynamically active doses of PB2452 were administered, we saw immediate and complete reversal of ticagrelor's antiplatelet activity based upon restoration of platelet function. In 11 out of 12 subjects, platelet function was restored at the first measured time point at the end of the 30-minute infusion. The duration of reversal varied from approximately one to four hours depending upon the dose level and subject, with longer duration at higher doses. In cohort 7, we modified the dosing regimen to deliver a total dose of 18 g, with 3 g delivered in the first five minutes of infusion, followed by 15 g delivered at a constant rate over an additional 7 hours and 55 minutes. In cohort 7, we observed that all subjects achieved complete and sustained restoration of platelet function within two hours after the start of infusion. The duration of reversal in cohort 7 lasted approximately 16 hours from the start of the infusion as measured by restoration of platelet activity.

In cohorts 8, 9 and 10, the dosing regimen of PB2452 was further refined to achieve both a more rapid onset of reversal and a longer duration of reversal compared to earlier cohorts. We administered a total dose of 18 g, with the initial 6 g delivered as a bolus in cohorts 8, 9 and 10. The remaining 12 g was administered after the initial bolus for an additional 12 to 16 hours in cohorts 8, 9 and 10. In each of these cohorts, we observed both immediate and complete reversal within the first five minutes following initiation of infusion and a sustained duration of reversal of over 20 hours. We intend to further evaluate the dose and dosing regimens observed in these cohorts in future clinical trials.

Future Clinical Development Plans

We intend to initiate a Phase 2a clinical trial of PB2452 in healthy older subjects in the first half of 2019 in order to evaluate safety and efficacy of PB2452 in this population. Older adults may exhibit more variability in drug response to ticagrelor and potentially higher levels of baseline platelet reactivity compared to younger subjects, and they resemble the patient population most likely to be treated with ticagrelor who could potentially benefit from PB2452, if approved. We anticipate that this trial will be a randomized, double blind, sequential, four-cohort, single dose trial. We intend to design the Phase 2a trial to identify the most appropriate dose and dosing regimen of PB2452 for our planned Phase 2b and Phase 3 clinical trials.

In mid-2019, we intend to request a meeting with the FDA to review the clinical profile of PB2452 and confirm our later phase development plans. Subject to discussions with the FDA, we intend to initiate a multi-center Phase 2b clinical trial in the second half of 2019 in healthy older subjects aged 50 to 80 who have been pre-dosed with ticagrelor in order to assess the safety, tolerability and efficacy of the dose and dosing regimen of PB2452 established in our Phase 1 and Phase 2a clinical trials. Like the Phase 2a trial, these subjects will be enrolled in the Phase 2b trial because they are closer in age to the patient population most likely to be treated with ticagrelor and potentially benefit from PB2452. We expect that the trial will be conducted with a pre-specified interim analysis after an initial subset of subjects has been treated with PB2452.

Based upon confirmation of the dose and dose regimen in healthy older subjects, we intend to initiate a multi-center Phase 3 clinical trial designed to assess the effectiveness of PB2452 as a reversal agent in patients on ticagrelor who are experiencing a major bleeding event or who require urgent surgery. The FDA's accelerated approval regulations allow drugs that are being developed to treat an unmet medical need for serious conditions to be approved substantially based on evidence of an effect on a surrogate biomarker endpoint that is considered reasonably likely to predict clinical benefit, rather than a clinical endpoint such as survival or irreversible morbidity. If considered appropriate by the FDA, we intend to pursue accelerated approval of PB2452, which would allow us to submit a BLA prior to completion of the Phase 3 clinical trial based on restoration of platelet aggregation as a biomarker in an initial subset of the Phase 3 patients. If we were to receive accelerated approval, the completion of the Phase 3 clinical trial would likely be a post-marketing commitment.

PB2452 Preclinical Studies

In preclinical studies conducted by AstraZeneca, it was observed that PB2452 rapidly removed free ticagrelor and restored normal platelet aggregation and normal bleeding time. In a preclinical model of pigs pre-dosed with ticagrelor and aspirin, circulating levels of ticagrelor dropped by over 100-fold when measured five minutes after the administration of PB2452 and remained below the limit of quantitation for at least four hours. It was further observed in this model that dosing with ticagrelor and aspirin resulted in a 90% reduction in platelet aggregation. A single administration of PB2452 reversed and restored over 50% of ADP-induced platelet aggregation activity within five minutes and over 80% in one hour.

It was also observed that PB2452 reduced bleeding that had previously increased due to the presence of ticagrelor. In mice pre-dosed with ticagrelor, bleeding was initiated by a tail cut and bleeding time and total blood loss were measured. Mice treated with ticagrelor had a 4.3-fold increase in median blood loss and a 1.7-fold increase in median bleeding time versus untreated control mice. A single administration of PB2452 reduced circulating levels of free ticagrelor below the limit of quantification and blood loss and bleeding time were reduced to levels that were not significantly different to the untreated control group.

PB1046 for the Treatment of Pulmonary Arterial Hypertension

We are developing our second product candidate, PB1046, as a once-weekly novel treatment for PAH. PB1046 is based on our proprietary ELP half-life extension technology. We are currently conducting a Phase 2b clinical trial in PAH patients to assess the safety, tolerability and efficacy of PB1046. We have received two orphan drug designations for PB1046 from the FDA, one for the treatment of PAH and a second for cardiomyopathy associated with DMD. In February 2018, we received Small Business Innovation Research, or SBIR, grants from the National Institutes of Health in an aggregate amount of \$2.8 million to support the clinical development of PB1046 for the treatment of PAH for the period from February 17, 2018 to July 31, 2020. In connection with the SBIR grants, the U.S. government will receive a non-exclusive, royalty-free license to use any technology we develop under such grants. As of December 31, 2018, we had recognized \$0.7 million of grant revenue under the SBIR grants.

Background on PAH

PAH is a progressive and life-threatening orphan disease with no known cure. Common symptoms, which worsen as the disease progresses, include shortness of breath, fatigue, angina, fainting, light headedness and abdominal distension. The disease is caused by abnormal constriction and adverse remodeling of the arteries and is characterized by high blood pressure in the pulmonary arteries, the blood vessels leading from the heart to the lungs. This pressure restricts blood circulation through the lungs resulting in poor oxygenation, abnormal strain on the heart's right ventricle and underfilling of the left ventricle. Over time, the remodeling worsens as inflammatory cells are recruited. This leads to tissue scarring and fibrosis, which results in severe restriction of blood flow, increasing the risk of developing life-threatening blood clots, heart failure and premature death.

The clinical severity of PAH is classified according to a system originally developed for heart failure by the New York Heart Association and then modified by the World Health Organization for patients with PAH, ranging from functional class I (no symptoms) through functional class IV (severe symptoms). Most standard of care therapy is initiated in patients who have progressed to class II or beyond.

According to the Pulmonary Hypertension Association, there are approximately 30,000 patients diagnosed with PAH in the United States. There are several approved therapies for PAH, and patients initially start treatment with a combination of two oral therapies. While advances in the treatment of PAH over the last two decades have markedly improved median survival from 2.8 years to approximately 9 years after diagnosis, PAH patients still face significant burdens from their disease and premature death. We estimate, based on publicly disclosed product sales data, that 2013 combined global sales for PAH therapies were approximately \$4.5 billion. Product sales have expanded by more than 30% since 2013 and continue to grow.

Limitations of Current Therapies for PAH

There is currently no cure for PAH. The three classes of currently approved drugs for the treatment of PAH are all systemic vasodilators that directly modulate vasoconstrictive or vasodilatory pathways. These currently approved therapies for PAH focus on three distinct molecular pathways: the endothelin pathway, the nitric oxide pathway and the prostacyclin pathway. The classes of drugs that target these three pathways are:

- **Endothelin Receptor Antagonists.** Endothelin receptor antagonists work by blocking the action of endothelin-1, a potent vasoconstrictor, thereby increasing blood flow to the lungs. These drugs, which are delivered orally, include bosentan and macitentan, marketed by Actelion as Tracleer and Opsumit, and ambisentan, marketed by Gilead as Letairis.
- **Nitric Oxide Pathway Modulators.** Nitric oxide is a naturally occurring molecule that is widely recognized as important in a number of biological processes. Nitric oxide causes blood vessels to relax and widen, resulting in an increase in blood flow. Oral drugs such as sildenafil, marketed by Pfizer as Revatio, and tadalafil, marketed by United Therapeutics as Adcirca, are phosphodiesterase type 5 inhibitors that work by enhancing the activity of naturally occurring nitric oxide.
- **Prostacyclin Analogues and IP Prostacyclin Receptor Agonists.** Patients with PAH have been shown to have reduced levels of prostacyclin, a naturally occurring substance that relaxes the pulmonary blood vessels, prevents platelet aggregation and inhibits the proliferation of smooth muscle cells in the pulmonary vessels. Prostacyclin analogues and IP prostacyclin receptor agonists, such as iloprost, treprostinil and selexipag, marketed by Bayer and Actelion as Ventavis, United Therapeutics as Remodulin and Actelion as Uptravi, respectively, mimic the effects of prostacyclin and are approved therapies for PAH.

These drugs have been shown to improve exercise capacity, quality of life, pulmonary arterial pressure and short-term survival in PAH patients and suggest enhanced long-term survival based on observational studies. However, none of the current treatments is curative and long-term prognosis remains poor. These therapies have a singular approach to treating PAH by modulating the vasoconstrictive or vasodilatory pathways but have limited ability to address other disease processes such as inflammation, cell proliferation, fibrosis and vascular remodeling. Furthermore, these drugs can cause hypotension, which can cause fainting and dizziness and can be life-threatening. As the disease progresses, additional vasodilator therapies are typically added to existing therapies rather than replacing drugs that are no longer providing sufficient benefit.

Our Solution: PB1046

PB1046, a novel, subcutaneously-injected VIP analogue, is a recombinant fusion protein composed of VIP and our proprietary ELP half-life extension technology. Based on the pharmacokinetic profile of PB1046 observed in our clinical trials, the fusion of VIP to ELP results in both a longer circulating half-life and a prolonged absorption profile, potentially enabling once weekly dosing. We believe that, in addition to vasodilation, PB1046 may suppress the adverse remodeling of blood vessels and increase cardiac contractility and relaxation. PB1046 has been administered to more than 60 patients with hypertension or a history of cardiac disease in three Phase 1/2 clinical trials conducted in the United States with no drug-related SAEs to date.

PB1046 Background

VIP is a peptide hormone produced in many tissues throughout the body. Native VIP exerts its function in the body by binding to two distinct receptors: vasoactive intestinal peptide receptor 1, or VPAC1, and vasoactive intestinal peptide receptor 2, or VPAC2. As is the case for many other peptide hormones, the body uses VIP for distinct purposes in different locations. VPAC1 is found predominantly in the gastrointestinal tract, while VPAC2 is found predominantly in the myocardial wall and pulmonary arteries. VIP plays a key role in the relaxation of smooth muscles, which in turn leads to the dilation of blood vessels and to the lowering of arterial blood pressure. VIP also inhibits airway and pulmonary vascular smooth muscle cell proliferation and has broad anti-inflammatory properties, in addition to neutralizing a variety of pulmonary vasoconstrictors, including endothelin.

We designed PB1046 using our ELP technology to harness the positive therapeutic effects of native VIP while addressing the drawbacks that make native VIP inappropriate for use as a direct therapy. Native VIP is rapidly degraded, and, when injected into the body, is eliminated within minutes, limiting its therapeutic effect. High levels of native VIP also result in severe gastrointestinal problems due to VPAC1 activation. We have used our ELP technology to extend the half-life of VIP in PB1046 to approximately 60 hours. In addition, we designed PB1046 to be active predominantly on VPAC2 rather than VPAC1 in order to preferentially affect the lung and cardiac tissue and reduce the potential for gastrointestinal side effects associated with VPAC1 activation.

Clinical Development of PB1046

We have completed two clinical trials of subcutaneously-injected PB1046. In these trials, PB1046 was observed to be well tolerated, with no drug-related SAEs. In both trials, we observed that patients receiving PB1046 experienced reductions in blood pressure that were sustained for at least one week, with no reported episodes of symptomatic hypotension.

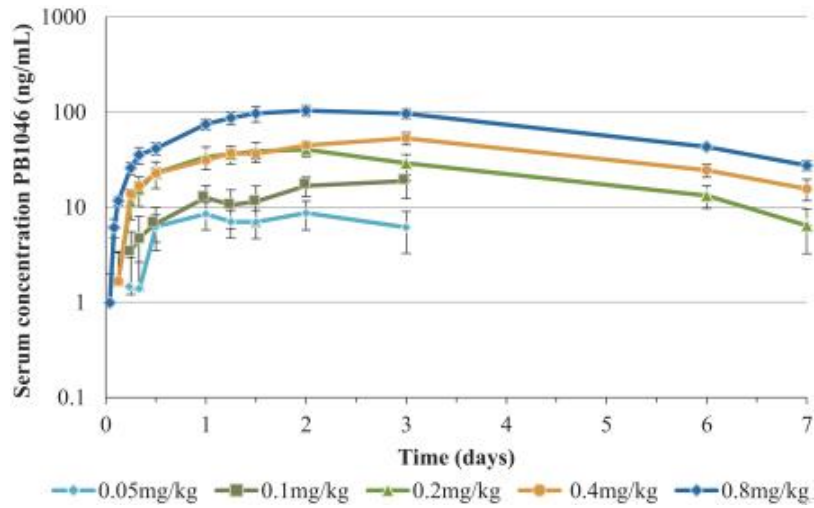
PB1046 Phase 2b Clinical Trial

We are conducting a randomized, double-blinded, controlled Phase 2b trial with an open-label extension in approximately 60 patients with PAH who are functional class II or III. In this trial, patients receive weekly subcutaneous injections of PB1046, in addition to their oral standard of care medications, for 16 weeks. These patients initially receive a dose of 0.2 mg/kg of PB1046, to be escalated and ultimately increased to a maximum dose of 2.0 mg/kg, as tolerated. Because in earlier clinical trials we have observed an association between PB1046 dosing and injection site erythema, in lieu of a completely inactive placebo, we instead use a blinded control that has a very low dose of PB1046 that is below a level likely to have therapeutic benefit but still produces local vasodilation at the injection site in most subjects. The primary endpoint is the change in pulmonary vascular resistance as measured by invasive right heart catheterization. Secondary endpoints include six minute walk distance, respiratory function and biomarkers for cardiac function. Safety endpoints include incidence and severity of AEs and immunogenicity. Six minute walk distance is an important clinical endpoint that the FDA has previously used as the basis for approval of other PAH drugs. We expect to report results from this clinical trial in 2020.

Phase 1 Single Ascending Dose Clinical Trial

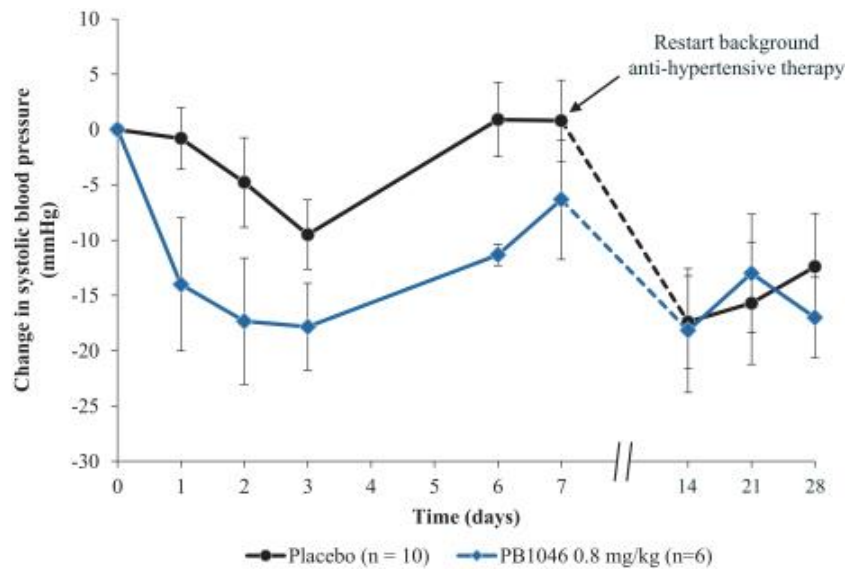
We have completed a single ascending dose Phase 1 clinical trial of subcutaneously injected PB1046 in 30 patients with hypertension to assess the safety and pharmacokinetics of PB1046 and to demonstrate early proof of concept. In this clinical trial, the patients stopped taking their standard of care anti-hypertensive medications for 14 days before receiving either placebo or a single ascending dose of PB1046 of between 0.05 mg/kg and 0.8 mg/kg. Consistent with our expectation for slow release of ELP fusion proteins, the half-life of PB1046 was approximately 60 hours and serum levels of PB1046 exhibited a prolonged pharmacokinetic profile extending to at least seven days following a single subcutaneous dose, as illustrated below. This is in contrast to the pharmacokinetics of native VIP in which serum levels of VIP disappear within minutes. We believe these results support once weekly subcutaneous dosing of PB1046.

Pharmacokinetics of single subcutaneous doses of PB1046 in a Phase 1 dose escalation trial



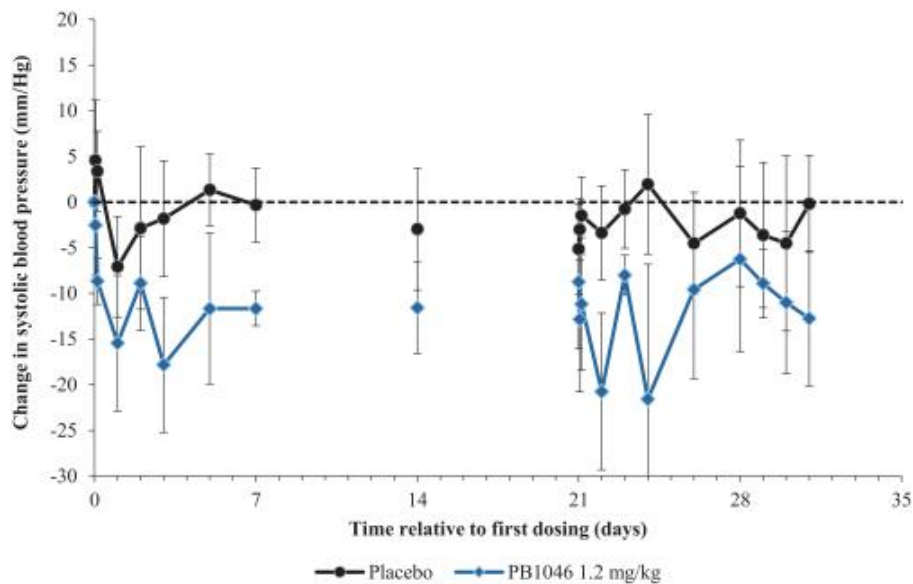
The pharmacodynamic activity of PB1046 was assessed by measurements of changes in blood pressure. In the highest dose cohort, we observed that systolic and diastolic blood pressure in patients receiving PB1046 were reduced within one day and remained below levels seen in placebo-treated patients for seven days, as illustrated below. At seven days, all patients resumed their standard hypertension medications and subsequent blood pressures, and the magnitude of reduction in blood pressure compared to baseline, were similar whether they had received PB1046 or placebo.

Mean change in systolic blood pressure in a Phase 1 trial following single subcutaneous dose of PB1046



We conducted a double-blinded, multiple ascending dose Phase 1b/2a trial in 29 patients with heart failure with reduced ejection fraction, or HFrEF, in order to assess the safety and long-acting pharmacokinetic and pharmacodynamic activity of subcutaneously injected PB1046 in patients with cardiovascular disease. In HFrEF, the heart muscle is not able to contract adequately and therefore expels less oxygen-rich blood into the body. In this clinical trial, patients remained on their standard of care heart failure medications and received either weekly placebo or weekly multiple ascending doses of PB1046 of between 0.2 mg/kg and 1.2 mg/kg for four weeks. This clinical trial reproduced the safety, pharmacokinetic and pharmacodynamic observations of the single dose trial, and we observed that once weekly dosing was well tolerated. No drug-related SAEs were reported, and there were no reported instances of hypotension, excluding mild orthostatic hypotension in four subjects, which did not appear to be dose related. Of the 22 subjects who received active study drug, all experienced injection site erythema reaching severe toxicity due to the size of the erythema, and three subjects discontinued treatment due to the erythema. We observed that patients in the highest dose cohort had a statistically significant reduction in blood pressure compared to placebo that was sustained throughout the dosing period, with p-value of 0.043, as illustrated below. A result is considered to be statistically significant when the probability of the result occurring by random chance, rather than from the efficacy of the treatment, is sufficiently low. The conventional method for determining the statistical significance of a result is known as the “p-value,” which represents the probability that random chance caused the result (e.g., a p-value = 0.01 means that there is a 1% probability that the difference between the control group and the treatment group is purely due to random chance). Generally, a p-value less than 0.05 is considered statistically significant.

Mean change in systolic blood pressure in a Phase 1b/2a trial following four weekly subcutaneous doses of PB1046

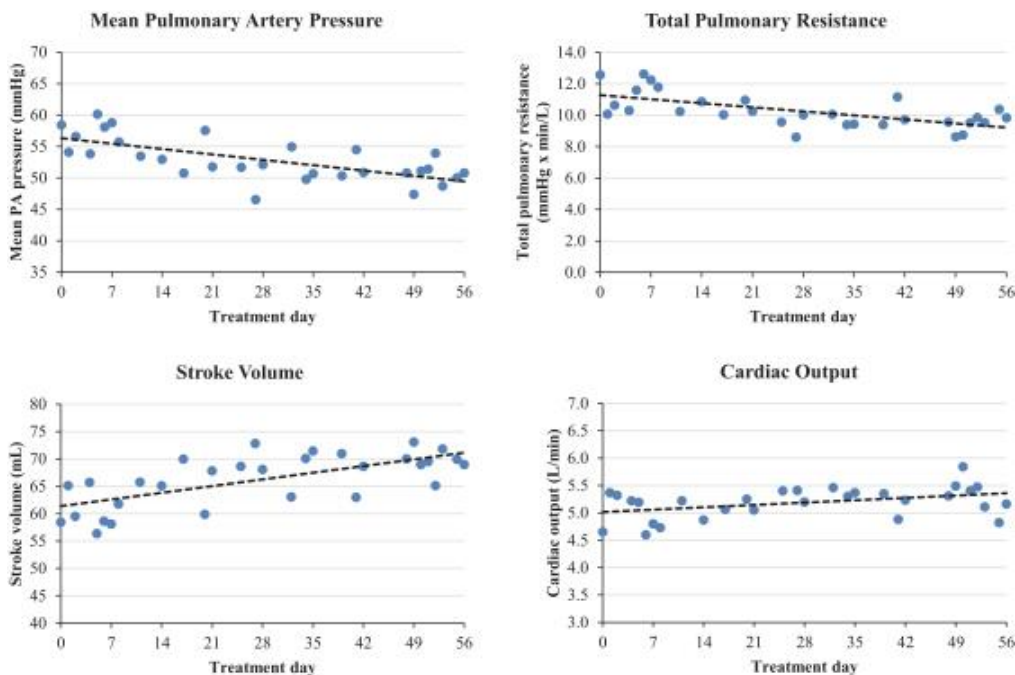


Based on the results of this clinical trial, and an assessment of a number of clinical and commercial factors, we determined that our initial indication for PB1046 would be PAH.

Prior to launching a large Phase 2b trial in patients with PAH, the FDA requested that we explore the safety and hemodynamics of PB1046 in patients with PAH. To achieve this objective, we initiated a pilot Phase 1b/2a clinical trial in a small population of PAH patients who had an implanted CardioMEMS device. The patients enrolled in this trial were difficult-to-treat patients with long histories of PAH who were no longer responding to their current therapies. These patients initially received a dose of 0.2 mg/kg of PB1046, which was escalated weekly as tolerated and could be increased to a maximum dose of 2.0 mg/kg, while remaining on their existing therapies.

In the first two patients dosed in this clinical trial, we observed changes in parameters that are important to PAH patients, including that patients' pulmonary arterial pressure and pulmonary resistance decreased over time while cardiac stroke volume and overall cardiac output increased. Results for one of the patients in this trial are illustrated below. The results from the second patient were generally consistent with this patient. These observations are consistent with our expectations for a VIP-based therapy. These patients had continued improvements over a period of 60 days, which we believe suggest that, in addition to its vasodilatory activity, PB1046 may also have more long-term effects on blood vessel and cardiac remodeling. These patients also opted into a trial protocol extension.

Representative CardioMEMS data from one PAH patient receiving weekly doses of PB1046



In subsequent discussions with the FDA, the safety profile of our Phase 1b/2a clinical trial and the available data from this pilot clinical trial were reviewed, and the FDA determined that our data were sufficient to enable initiation of a Phase 2b clinical trial. Accordingly, we do not intend to enroll additional patients in this pilot clinical trial.

Safety Overview from Clinical Trials of PB1046

There were no drug-related SAEs reported for any of the patients who have received PB1046. When PB1046 was administered subcutaneously, it was almost always associated with a mild- to moderate-injection site erythema, or patch of redness, which on average appeared at about 12 hours after injection. The injection site erythema was not judged by the investigator to be an allergic type reaction; rather, in the investigator's view, it was likely to be associated with the activity of VIP binding to receptors in the skin, resulting in local vasodilation. Additionally, 70% of patients receiving a subcutaneous injection of PB1046 experienced mild pain or tenderness at the injection site, which occurred hours to days after injection and on average lasted about one week. One-third of the patients also experienced mild pruritus, or itching, at the site of injection. We believe that these events are primarily due to the fused VIP peptide since similar events were not observed in clinical trials of other constructs that contain the ELP domain. None of the injection site reactions were judged to be serious. We have also completed a Phase 1 clinical trial with intravenously administered PB1046 in which we observed a similar tolerability profile. Notably, there were no events of symptomatic hypotension related to PB1046 in any of the subjects who have received PB1046.

Preclinical Studies

Published independent research indicates that patients with PAH have both reduced levels of VIP in the lung and in circulation as well as increased levels of VPAC2 receptors in lung tissue. Mice bred to be VIP-deficient spontaneously express symptoms of moderately severe PAH. Repeated treatment of these mice with VIP corrected the key characteristics of the disease including right heart dysfunction, vascular remodeling and lung inflammation. In the monocrotaline-induced PAH rat model, an experimental model of PAH, VIP was active in preventing, and partially reversing, the symptoms of PAH. Combination therapy with VIP and the endothelin receptor antagonist bosentan was shown to be more active than either drug alone. Furthermore, in multiple preclinical studies we have demonstrated the benefits of PB1046 in cardiomyopathies, due to its ability to induce heart contractility and relaxation effects without an increase in myocardial oxygen demand.

Potential Applications of PB1046 in Other Indications

The biological activities associated with VIP have the potential to provide therapeutic benefit to patients with other diseases. We believe that PB1046 provides a mechanism to bring these VIP-based therapies forward in the following indications:

- **DMD-associated Cardiomyopathy.** Cardiac dysfunction is a very common manifestation of DMD and a common cause of death for individuals with this condition. The ability of PB1046 to increase contractibility of cardiac muscles presents the possibility that it could provide therapeutic benefit to these patients. We observed that PB1046 slowed deterioration in cardiac function and preserved skeletal muscle function in a mouse model of DMD. In addition to direct effects on cardiac function, we believe decreased fibrosis also contributed to the positive effects of PB1046 on both cardiac and skeletal muscle in this model.
- **Cystic Fibrosis.** VIP has been shown to stimulate the processing of cystic fibrosis transmembrane regulator, or CFTR, the protein defective in patients with cystic fibrosis, or CF. In mice lacking the gene for VIP, CFTR is not located at the cell surface, where it is required to function properly, but accumulates within the cell. These mice have lung abnormalities that resemble CF and treatment with VIP peptide restored CFTR to the cell surface and corrected the lung tissue abnormalities. Treatment of human epithelial cells containing the most common CFTR mutation found in patients with CF, F508del, with PB1046 has been observed to increase CFTR activity, providing further support that PB1046 may have potential as a treatment for patients with CF.

ELP Technology

Our proprietary ELP technology is based on recombinant biopolymers called ELPs, which comprise individual subunits or building blocks derived from a five-amino acid repeat motif found in the human protein elastin. This five-amino acid motif is repeated multiple times to form the ELP biopolymer. We produce our ELP-based products by engineering *E. coli* to produce a single protein comprising the active peptide or protein fused to the ELP biopolymer. This molecule is active as a fusion protein and does not require cleavage or release of the peptide. ELP fusion proteins are produced in the soluble fraction of *E. coli*, which allows for ease of scale-up and purification.

Fusion to ELPs significantly improves the stability of peptides and proteins and enables use of natural or minimally altered peptide sequences. We believe these fusion proteins retain similar potency to the native molecule while being protected from degradation by enzymes in circulation. Additionally, we have observed that the fusion protein maintains the solubility and long half-life of the ELP, in many cases allowing for long-term liquid stability, which is important for injectable products.

ELP fusion proteins can undergo a reversible phase transition, in which ELP fusion proteins aggregate and form a sustained-release depot under the skin. This phase transition is driven by changes in temperature. At lower temperatures ELP fusion proteins are completely soluble, while at warmer temperatures the ELP fusion proteins are in a gel-like state. This allows the ELP fusion proteins to be easily handled and administered subcutaneously using standard, fine gauge needles and syringes. Once the ELP fusion protein is exposed to body heat, it forms a drug depot that slowly releases soluble ELP fusion protein into circulation. By modifying the amino acid sequence of the individual subunits and by varying its overall length, we can engineer our ELP fusion proteins to be released on timescales extending to a week or longer.

Product candidates based on our ELP technology, including prior product candidates that we ceased development of in order to focus on the development of therapies for orphan diseases, have been evaluated in over 500 patients with no known drug-related SAEs.

Preclinical Programs

We continue to invest in applying our ELP technology to the development of novel product candidates. Our focus is on peptides and proteins that are scientifically or clinically validated but where a suboptimal half-life, stability and delivery limit their potential therapeutic applications.

Our more advanced preclinical programs include:

- **Glucagon-like peptide-2.** Glucagon-like peptide-2, or GLP-2, stimulates growth of intestinal villi, increasing their ability to absorb nutrients. GLP-2 is a potential treatment for patients with short bowel syndrome, Crohn's disease or mucositis in patients undergoing cancer treatment. Teduglutide, currently marketed under the brand name Gattex, is an FDA-approved therapy based on GLP-2 that requires daily injections. In animal models, our GLP-2-ELP product candidate provided sustained levels of GLP-2, resulting in greater efficacy than teduglutide with less frequent dosing.
- **C-type natriuretic peptide.** C-type natriuretic peptide, or CNP, is a regulator of bone growth and can rescue defects in fibroblast growth factor 3 that cause achondroplasia resulting in dwarfism. Native CNP has a half-life of less than three minutes, limiting its use as a direct therapeutic. We are developing our CNP-ELP product candidate to deliver therapeutic levels of CNP with once weekly subcutaneous injections. In a mouse model, we observed a demonstrated effect on linear growth when our CNP-ELP product candidate was injected once every four days.

License Agreements

MedImmune Limited

In November 2017, we entered into an exclusive license agreement with MedImmune, a wholly owned subsidiary of AstraZeneca, or the MedImmune License. Pursuant to the MedImmune License, MedImmune granted us an exclusive, worldwide license under certain patent rights owned or controlled by MedImmune to develop and commercialize any products covered by the MedImmune License, or the MedImmune licensed products, for the treatment, palliation, diagnosis or prevention of any human disorder or condition. The in-licensed patent rights are generally directed to antibodies that bind to ticagrelor and methods of use and include one issued patent in the United States, three pending patent applications in the United States and 13 pending foreign applications. The last patent is expected to expire in 2036 without extension. We have the right to sublicense the licensed technology to third parties subject to certain conditions as specified in the MedImmune License. Under the MedImmune License, we grant to MedImmune a worldwide, non-exclusive, royalty-free, irrevocable license and right of reference solely to exploit any drug product containing ticagrelor or any invention, discovery, development or modification with respect to any drug product containing ticagrelor.

Under the terms of the MedImmune License, we have paid or are required to pay:

- an upfront fee of \$0.1 million;
- quarterly fees relating to technical services provided by MedImmune;
- up to \$18.0 million upon the achievement of certain clinical and regulatory milestones;
- up to \$50.0 million upon the achievement of certain commercial milestones; and
- mid-single digit to low-teen royalty percentages on net sales of MedImmune licensed products, subject to reduction in specified circumstances.

As of December 31, 2018, we have paid \$0.5 million under the MedImmune License, related to third-party product storage costs.

The MedImmune License requires us to use commercially reasonable efforts to develop, obtain and maintain regulatory approval for and commercialize the MedImmune licensed products throughout the term of the MedImmune License. We have the first right, but not the obligation, to control prosecution of the in-licensed patents. In addition, our rights under the MedImmune License are not assignable without the prior written consent of MedImmune, except to a third-party acquirer by our merger or sale of our stock or assets or to an affiliate of our company.

Unless earlier terminated, the MedImmune License automatically expires on the date on which we no longer owe any royalty payments to MedImmune under the MedImmune License, which date will occur on the later of (1) the tenth anniversary of the first commercial sale of the MedImmune licensed products, (2) the expiration of the last in-licensed patent in 2036 and (3) the expiration of regulatory exclusivity under the MedImmune License. The MedImmune License may be terminated prior to its expiration:

- by mutual written consent of us and MedImmune;
- by either party upon the other party's material breach of the MedImmune License that is not cured within the specified cure period based on the nature of such breach;
- by either party in the event of either party's bankruptcy, insolvency or certain similar occurrences;
- by MedImmune if we bring any action or proceeding challenging the validity or enforceability of any of the licensed patents;
- by us, under specified circumstances, if we believe in good faith that there is (1) an issue with respect to the safety or efficacy of PB2452 or any MedImmune licensed product containing PB2452 or (2) an issue with respect to the commercial viability of any MedImmune licensed products, in each case subject to dispute resolution by an independent expert; and
- by us, with respect to a particular country or region, if any product containing ticagrelor is withdrawn by a regulatory authority in such country or region.

Upon termination of the MedImmune License, we grant to MedImmune an exclusive, royalty-free, sublicensable license under our patent rights and know-how to use, sell, have sold, offer for sale, develop, make, have made, manufacture, commercialize, have used, import, export, transport, distribute, promote, market or otherwise dispose certain compounds or products covered by the MedImmune License.

Duke University

In October 2006, we entered into an exclusive license agreement, which was most recently amended in May 2017, with Duke University, or the Duke License. Pursuant to the Duke License, Duke granted to us an exclusive, worldwide license under certain patent rights and a non-exclusive license to know-how owned or controlled by Duke to develop and commercialize any products or processes covered under the Duke License, or the Duke licensed products. The in-licensed patent rights are generally directed to providing extended exposure for proteins and peptides administered through subcutaneous injections and include 13 registered patents in the United States, seven registered patents in foreign jurisdictions, three pending patent applications in the United States and seven pending foreign applications. The last patent is expected to expire in 2030 without extension.

We have the right to sublicense the Duke licensed products to third parties subject to certain conditions specified in the Duke License. In May 2017, certain patent rights under the Duke License reverted to Duke, and Duke subsequently granted to us a non-exclusive license under such patent rights to develop and commercialize any products or processes involving such patent rights. We also granted back to Duke an exclusive sublicense under certain patent rights licensed to us under the Duke License and a non-exclusive license under certain patent rights owned or controlled by us, in each case to exploit compounds developed using our proprietary ELP technology.

Under the terms of the Duke License, we have paid or are required to pay:

- an upfront fee of \$37,000;
- amendment fees of \$0.2 million related to subsequent amendments of the Duke License;
- additional licensing fees of \$0.2 million;
- up to \$2.2 million in clinical and regulatory milestone fees;
- up to \$0.4 million in commercial milestone fees;
- low single-digit royalty percentages on net sales of Duke licensed products, with minimum aggregate royalty payments of \$0.2 million payable following our achievement of certain commercial milestones; and
- up to the greater of \$0.3 million or a low double-digit percentage of the fees we receive from a third party in consideration of forming a strategic alliance with respect to certain patent rights covered under the Duke License.

In consideration for license rights granted to us, we initially issued Duke 24,493 shares of our common stock. Until we reached a certain stipulated equity milestone, which we reached in October 2007, we were obligated to issue additional shares of common stock to Duke from time to time so that its aggregate ownership represented 7.5% of our issued and outstanding capital stock.

As of December 31, 2018, we have not paid any amounts under the Duke License. As of May 2017, Duke is required to pay us a percentage of revenue that it receives from granting a license or sublicense with respect to certain products covered under the Duke License. As of December 31, 2018, Duke has not paid us any of such fees. We also must pay Duke the first \$1.0 million of non-royalty payments we receive from a sublicensee, and thereafter a low double-digit percentage of any additional non-royalty payments we receive.

The Duke License requires us to use commercially reasonable efforts to develop, obtain and maintain regulatory approval for and commercialize the Duke licensed products according to a particular development schedule throughout the term of the Duke License. We are required to apply for, prosecute and maintain all U.S. and foreign patent rights under the Duke License. In addition, our rights under the Duke License are not assignable without the prior written consent of Duke, except to a third-party acquirer by our merger or sale of our stock or assets, or to an affiliate of our company.

Unless earlier terminated, the Duke License automatically expires on the date on which all patent rights granted under the Duke License expire, or upon our bankruptcy, insolvency or certain similar occurrences. The Duke License may be terminated prior to its expiration:

- by mutual written consent of us and Duke;
- by us upon three months' written notice to Duke;
- by either party upon the other party's illegal conduct or guilty plea with respect to intentional fraud, willful misconduct or felony;
- by either party upon the other party's material breach of the Duke License that is not cured within the specified cure period based on the nature of such breach; and
- by Duke upon our decision to cease commercial development of the patent rights covered by the Duke License for a material period of time.

Upon termination of the Duke License, we grant to Duke an exclusive, royalty-free, sublicensable license under our patent rights and know-how to use any intellectual property developed by us in the course of exercising our rights under the Duke License.

Manufacturing

Our clinical and preclinical product candidates are currently manufactured using a microbial expression system. Our manufacturing utilizes a straight-forward *E. coli* fermentation process with a simple column chromatography-based purification process. We believe that these manufacturing processes will enable our product candidates to be manufactured efficiently for clinical and commercial applications. We do not have any cGMP manufacturing facilities. Instead, we utilize third parties for the cGMP manufacture of our product candidates for clinical trials, and we intend to continue to use third parties in the near term for the future clinical development and, if they are approved, commercial manufacture of our drug products. Our contract manufacturers are FDA-inspected establishments that have a history of supplying products to the pharmaceutical industry in accordance with cGMP.

PB2452

PB2452 bulk drug substance, provided to us pursuant to the MedImmune License, was filled and released for use in our Phase 1 clinical trial. The PB2452 drug substance was manufactured by Wacker Biotech GmbH, or Wacker, a third-party contract manufacturer, utilizing Wacker's proprietary *E. coli* strain. Manufacturing has continued at Wacker to generate drug supply for our planned Phase 2a and Phase 2b clinical trials. We have engaged BioVectra, Inc. to serve as our contract manufacturer of PB2452 for later-stage clinical trials and, if approved, commercial-scale production. As we advance PB2452 through clinical development, we may establish additional supply agreements for the manufacture of PB2452 in order to meet our expected needs for potential commercial demand.

PB1046 and our ELP Preclinical Pipeline

To date, we have relied on a non-proprietary *E. coli* strain for the production of PB1046 and our preclinical ELP pipeline candidates. Third-party manufacturers have performed the cGMP manufacturing of the drug product. Due to efficiencies achieved to date, we intend to utilize this non-proprietary strain for future manufacturing. As we advance PB1046 and other preclinical product candidates through development, we intend to establish additional supply agreements and/or technology transfer agreements in order to meet our expected needs for future clinical trials and potential commercial demand.

Sales and Marketing

We retain worldwide commercial rights to all of our product candidates. Given our stage of development, we have not yet established a commercial organization or distribution capabilities. We intend to commercialize PB2452, if approved, independently in the United States because we believe the patient populations and medical specialists for these indications are sufficiently concentrated to allow us to effectively promote these products with a targeted sales team. We may explore, and selectively pursue, strategic collaborations or partnerships with third parties to commercialize PB1046, if approved, in the United States and any approved products outside of the United States in order to maximize the commercial potential of our products.

Competition

The pharmaceutical industry is subject to rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing treatments and new treatments that may become available in the future.

Our current and potential future competitors have significantly more experience commercializing drugs that have been approved for marketing. Mergers and acquisitions in the pharmaceutical and biotechnology industries could result in even more resources being concentrated among a small number of our competitors. Accordingly, our competitors may be more successful than us in obtaining regulatory approval for therapies and in achieving widespread market acceptance of their drugs. It is also possible that the development of a cure or more effective treatment method for the disorders we are targeting by a competitor could render our current or future drug candidates non-competitive or obsolete or reduce the demand for our drug candidates before we can recover our development and commercialization expenses.

PB2452

There are currently no known reversal agents approved or in clinical development for ticagrelor. As a result, market acceptance of PB2452, if approved, will depend heavily on the continued market acceptance and use of ticagrelor. Ticagrelor competes against other commercially available antiplatelet therapies, including other P2Y₁₂ receptor antagonists, many of which are available as generic drugs and are therefore currently significantly less expensive than ticagrelor. New antiplatelet therapies may also be developed in the future, including other reversible P2Y₁₂ receptor antagonists and other antiplatelet therapies, which could also have reversal agents, that could displace ticagrelor as the preferred antiplatelet agent for ACS.

PB1046

Although we anticipate that PB1046 may be used as a complement to patients' existing therapies, we expect to compete with existing treatments for PAH patients with class II through class IV symptoms that target the endothelin, nitric oxide and prostacyclin pathways, as well as any generic equivalents that may be developed. In addition to currently approved drugs within these classes, we are also aware of a number of PAH therapies in clinical development, including:

- *Ralinepag*, an oral IP prostacyclin receptor agonist being developed by Arena Pharmaceuticals;
- *Trevyent*, a formulation of treprostinil being developed by United Therapeutics;
- *Bardoxolone methyl*, an oral therapy being developed by Reata Pharmaceuticals for connective tissue disease-associated PAH;
- *LIQ861*, a powder formulation of treprostinil designed for deep-lung delivery using a disposable, dry powder inhaler being developed by Liquidia Technologies;
- *CAM2043*, a liquid crystal gel formulation of treprostinil as a once-weekly subcutaneous depot injection being developed by Camurus;

- *Treprostinil Technosphere*, an inhaled, dry powder formulation of treprostinil being developed by MannKind Corporation;
- *Beraprost sodium 314d modified release*, a single isomer oral prostacyclin analogue being developed by Lung Biotechnology PBC;
- *Sotatercept*, being developed by Acceleron;
- *GB002*, being developed by Gossamer Bio;
- *INS1009*, an inhaled nanoparticle formulation of a treprostinil prodrug being developed by Insmed Incorporated; and
- *INOpulse*, inhaled nitric oxide being developed by Bellerophon Therapeutics.

Intellectual Property

Our commercial success depends in part upon our ability to obtain and maintain proprietary protection for PB2452, PB1046 and future product candidates and related discoveries and our ELP technology; to operate without infringing on or otherwise violating the proprietary rights of others; and to prevent others from infringing or otherwise violating our proprietary rights. We seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our ELP technology, our product candidates and other proprietary technologies, inventions and improvements that are important to the development and implementation of our business. We also rely on trademarks, trade secrets, know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our proprietary position.

The term of individual patents varies depending on the date of filing of the patent application and the legal term of patents in the countries in which they are obtained. Generally, patents issued from regularly filed applications in the United States are granted a term of 20 years from the earliest filing date of a non-provisional application. In addition, in certain instances, a patent term can be adjusted to recapture a portion of the delay by the United States Patent and Trademark Office in issuing the patent. In addition, a patent term may be extended to recapture a portion of the patent term effectively lost as a result of the FDA regulatory review period of the drug covered by the patent. The patent term extension based upon delay by the FDA can 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 and the extension may only apply to one patent that covers the approved drug (and to only those patent claims covering the approved drug or a method for using it). There can be no assurance that any such patent term adjustment or extension will be obtained. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically in countries that we file, the patent term is 20 years from the earliest filing date of a non-provisional patent application. However, the actual protection afforded by a patent varies on a product-by-product basis, from country to country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

Furthermore, we rely upon trade secrets, know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our commercial partners, collaborators, employees and consultants and invention assignment agreements with our employees. We also have confidentiality agreements or invention assignment agreements with our commercial partners and selected consultants. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed through a relationship with a third party. These agreements may be breached and we may not have adequate remedies for any such breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our commercial partners, collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

As of December 31, 2018, our patent estate contained at least 15 patent families that we own or in-license which protects various aspects of our ELP technology or our product candidates. We own or have rights in 20 United States patents, over 10 United States patent applications, over 50 foreign patents and over 40 foreign patent applications.

PB2452

With regard to PB2452, we in-licensed one patent family. As of December 31, 2018, this patent family includes one issued U.S. patent with composition of matter claims covering PB2452 that is scheduled to expire in 2036 without taking patent term extensions into account, five pending U.S. patent applications and 13 pending foreign applications, that if issued, would expire in 2035. We are heavily dependent on the patented or proprietary technologies that we license from third parties.

PB1046

As of December 31, 2018, our portfolio of owned and in-licensed patents and patent applications relating to PB1046 consists of six issued patents in the United States, five pending applications in the United States, 16 granted foreign patents and 19 pending foreign applications with claims directed to compositions of matter covering PB1046 and methods of use thereof, including use in PAH, cystic fibrosis and cardiomyopathy associated with DMD, that we expect to expire between 2027 and 2036, without taking patent term extensions into account

ELP Technology

As of December 31, 2018, we owned two patent families relating to our ELP technology, which consists of one granted patent in the United States, one pending application in the United States and six pending foreign applications. The granted patent expires in 2021 without taking patent term extensions into account.

Government Regulation and Product Approval

The FDA and other regulatory authorities at federal, state and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring and post-approval reporting of biologics such as those we are developing. We, along with third-party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval or licensure of our product candidates.

The process required by the FDA before biologic product candidates may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and animal studies performed in accordance with the FDA's Good Laboratory Practices, or GLP, regulation;
- submission to the FDA of an IND, which must become effective before clinical trials may begin and must be updated annually or when significant changes are made;
- approval by an independent Institutional Review Board, or IRB, or ethics committee at each clinical site before the trial is commenced;
- performance of adequate and well-controlled human clinical trials to establish the safety, purity and potency of the proposed biologic product candidate for its intended purpose;
- preparation of and submission to the FDA of a BLA after completion of all pivotal clinical trials;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;

- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with cGMP and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency and of selected clinical investigation sites to assess compliance with Good Clinical Practices, or GCP; and
- FDA review and approval of the BLA to permit commercial marketing of the product for particular indications for use in the United States.

Preclinical and Clinical Development

Prior to beginning the first clinical trial with a product candidate, we must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND also includes results of animal and *in vitro* studies assessing the toxicology, pharmacokinetics, pharmacology and pharmacodynamic characteristics of the product; chemistry, manufacturing and controls information; and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site and must monitor the trial until completed. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some trials also include oversight by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board, which provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the trial and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical trials and clinical trial results to public registries.

For purposes of BLA approval, human clinical trials are typically conducted in three sequential phases that may overlap.

- Phase 1—The investigational product is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses and, if possible, to gain early evidence on effectiveness.
- Phase 2—The investigational product is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.

- Phase 3—The investigational product is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may be made a condition to approval of the BLA. Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the biological characteristics of the product candidate and must 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 product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product or, for biologics, the safety, purity and potency. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

BLA Submission and Review

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, nonclinical studies and clinical trials are submitted to the FDA as part of a BLA requesting approval to market the product for one or more indications. The BLA must include all relevant data available from pertinent preclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. The submission of a BLA requires payment of a substantial application user fee to FDA, unless a waiver or exemption applies.

Once a BLA has been submitted, the FDA's goal is to review standard applications within ten months after it accepts the application for filing or, if the application qualifies for priority review, six months after the FDA accepts the application for filing. In both standard and priority reviews, the review process is often significantly extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether a product is safe, pure and potent and the facility in which it is manufactured, processed, packed or held meets standards designed to assure the product's continued safety, purity and potency. The FDA may convene an advisory committee to provide clinical insight on application review questions. Before approving a BLA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced, 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 will describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the Complete Response letter without first conducting required inspections, testing submitted product lots and/or reviewing proposed labeling. In issuing the Complete Response letter, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the BLA with a Risk Evaluation and Mitigation Strategy, or REMS, to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a product and to enable patients to have continued access to such medicines by managing their safe use and could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase 4 post-marketing studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization and may limit further marketing of the product based on the results of these post-marketing studies.

Accelerated Approval Program

Any marketing application for a biologic submitted to the FDA for approval may be eligible for FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. A product is eligible for priority review if it has the potential to provide a significant improvement in the treatment, diagnosis or prevention of a serious disease or condition compared to marketed products. For biologic products, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date (compared with ten months under standard review).

Additionally, products studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, 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. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States for which there is no reasonable expectation that the cost of developing and making available in the United States a drug or biologic for this type of disease or condition will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting a BLA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. The orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review or approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusive approval (or exclusivity), which means that the FDA may not approve any other applications, including a full BLA, to market the same drug or biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Orphan drug exclusivity does not prevent FDA from approving a different drug or biologic for the same disease or condition or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA application fee.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Breakthrough Therapy Designation

To qualify for the breakthrough therapy program, product candidates must be intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence must indicate that such product candidates may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. The FDA will seek to ensure the sponsor of a breakthrough therapy product candidate receives: intensive guidance on an efficient drug development program; intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross-disciplinary review; and rolling review. Breakthrough therapy designation does not change the standards for approval but may expedite the development or approval process.

Post-Approval Requirements

Any products manufactured or distributed by us pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution and advertising and promotion of 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 user fee requirements, under which FDA assesses an annual program fee for each product identified in an approved BLA. Biologic manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Changes to the manufacturing process are strictly regulated and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

The FDA may withdraw 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 AEs of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of a product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of existing product approvals;
- product seizure or detention, or refusal of the FDA to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of biologics. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA 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. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

Biosimilars and Reference Product Exclusivity

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, signed into law in 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or the BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-approved reference biological product. To date, a number of biosimilars have been licensed under the BPCIA, and numerous biosimilars have been approved in Europe. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity and potency, can be shown through analytical studies, animal studies and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. Complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being worked out by the FDA.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, recent government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation and impact of the BPCIA is subject to significant uncertainty.

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

In addition to FDA restrictions on marketing of pharmaceutical products, federal and state healthcare laws and regulations restrict business practices in the biopharmaceutical industry. These laws may impact, among other things, our current and future business operations, including our clinical research activities and proposed sales, marketing and education programs and constrain the business or financial arrangements and relationships with healthcare providers and other parties through which we market, sell and distribute our products for which we obtain marketing approval. These laws include anti-kickback and false claims laws and regulations, data privacy and security and transparency laws and regulations, including, without limitation, those laws described below.

The federal Anti-Kickback Statute prohibits, among other things, individuals or entities from knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, overtly or covertly, in cash or in kind to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term “remuneration” has been broadly interpreted to include anything of value. The federal Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers and formulary managers on the other hand. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor.

In addition, a person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. Further, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act and the civil monetary penalties statute.

The federal civil and criminal false claims laws, including the False Claims Act, which prohibit, among other things, any individual or entity from knowingly presenting or causing to be presented, a false claim for payment to the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. A claim includes “any request or demand” for money or property presented to the U.S. government. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies’ marketing of products for unapproved, and thus non-reimbursable, uses.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. 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 it in order to have committed a violation.

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations, impose certain requirements relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization on certain health plans, healthcare clearinghouses and certain healthcare providers, known as covered entities, and their respective business associates, independent contractors that perform certain services involving the use or disclosure of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorneys’ fees and costs associated with pursuing federal civil actions.

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 Centers for Medicare & Medicaid Services, or CMS, information related to payments or other transfers of value made to physicians and teaching hospitals and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians and their immediate family members.

We may also be subject to state and foreign law equivalents of each of the above federal laws; state laws that require manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; state laws that require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or that otherwise restrict payments that may be made to healthcare providers; state and local laws that require the registration of pharmaceutical sales representatives; as well as state and foreign laws that 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 will comply with applicable healthcare laws and regulations will involve substantial costs. Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. 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 regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm and the curtailment or restructuring of our operations. To the extent that any of our products are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Coverage and Reimbursement

Market acceptance and sales of any drug products depend in part on coverage and the extent to which adequate reimbursement for drug products will be available from third-party payors, including government health administration authorities, managed care organizations and other private health insurers. Coverage and reimbursement for our product also depends on coverage and adequate reimbursement for the procedures using PB2452 as a ticagrelor reversal agent and PB1046 for the treatment of PAH. Obtaining coverage and adequate reimbursement for our products may be particularly difficult because of the higher prices often associated with drugs administered under the supervision of a physician. Separate reimbursement for the product itself or the treatment or procedure in which our product is used may not be available. Even if the procedure using our product is covered, third-party payors may package the cost of the drug into the procedure payment and not separately reimburse the physician for the costs associated with our product. A decision by a third-party payor not to cover or separately reimburse for our products could reduce physician utilization of our products once approved. Additionally, in the United States, there is no uniform policy of coverage and reimbursement among third-party payors. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. However, decisions regarding the extent of coverage and amount of reimbursement to be provided is made on a payor-by-payor basis. One payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage and adequate reimbursement.

Third-party payors determine which medical procedures they will cover and establish reimbursement levels. Even if a third-party payor covers a particular procedure, the resulting reimbursement payment rates may not be adequate. Patients who are treated in-office for a medical condition generally rely on third-party payors to reimburse all or part of the costs associated with the procedure and may be unwilling to undergo such procedures in the absence of such coverage and adequate reimbursement.

Reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that a procedure is safe, effective and medically necessary; appropriate for the specific patient; cost-effective; supported by peer-reviewed medical journals; included in clinical practice guidelines; and neither cosmetic, experimental, nor investigational.

Further, from time to time, typically on an annual basis, payment rates are updated and revised by third-party payors. Such updates could impact the demand for our product candidates, to the extent that customers who are prescribed our product candidates, if approved, are not separately reimbursed for the cost of the product candidates. An example of payment updates is the Medicare program updates to physician payments, which is done on an annual basis. In the past, when the application of the formula resulted in lower payment, Congress has passed interim legislation to prevent the reductions. The Medicare Access and CHIP Reauthorization Act of 2015, or MACRA, ended the use of the statutory formula and provided for a 0.5% annual increase in payment rates under the Medicare Physician Fee Schedule through 2019, but no annual update from 2020 through 2025. MACRA also introduced a merit based incentive bonus program for Medicare physicians beginning in 2019. At this time, it is unclear how the introduction of the merit based incentive program will impact overall physician reimbursement under the Medicare program.

Impact of Healthcare Reform on our Business

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of drug product candidates, restrict or regulate post-approval activities and affect the profitable sale of drug product candidates.

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. In March 2010, the ACA was passed, which substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry. The ACA, among other things: (1) established an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs; (2) expanded the entities eligible for discounts under the 340B drug pricing program; (3) increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively and capped the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price, or AMP; (4) expanded the eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability; (5) addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for certain drugs and biologics that are inhaled, infused, instilled, implanted or injected; (6) introduced a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; (7) created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and (8) established a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug.

Some of the provisions of the ACA have yet to be implemented, and there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the ACA. While Congress has not passed comprehensive repeal legislation, bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act of 2017, or Tax Act, includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. The Bipartisan Budget Act of 2018, or the BBA, among other things, amends the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." In July 2018, CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 2018, a Texas U.S. District Court Judge ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. While the Texas U.S. District Court Judge, as well as the Trump administration and CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the ACA will impact the ACA and our business.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013 and, due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2027 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have an adverse effect on customers for our product candidates, if approved, and, accordingly, our financial operations.

Additionally, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Further, the Trump administration released a "Blueprint," or plan, to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. The Department of Health and Human Services has already started the process of soliciting feedback on some of these measures and, at the same, is immediately implementing others under its existing authority. For example, in September 2018, CMS announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019, and in October 2018, CMS proposed a new rule that would require direct-to-consumer television advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product. Although a number of these and other proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

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

Employees

As of December 31, 2018, we had 24 employees, including 22 full-time employees. All of our employees are located in the United States. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Corporate Information

We were incorporated under the laws of the State of Delaware in January 2002. Our principal executive offices are located at 1 Great Valley Parkway, Suite 30, Malvern, Pennsylvania 19355. Our telephone number is (610) 981-6500. Our common stock is listed on the Nasdaq Global Market under the symbol "PHAS."

Available Information

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

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

Item 1A. Risk Factors.

The following information sets forth risk factors that could cause our actual results to differ materially from those contained in forward-looking statements we have made in this Annual Report on Form 10-K and those we may make from time to time. You should carefully consider the risks described below, in addition to the other information contained in this Annual Report on Form 10-K and our other public filings. Our business, financial condition or results of operations could be harmed by any of these risks. The risks and uncertainties described below are not the only ones we face. Additional risks not presently known to us or other factors not perceived by us to present significant risks to our business at this time also may impair our business operations.

Risks Related to Our Financial Position and Capital Needs

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

We are a clinical-stage biopharmaceutical company with a limited operating history.

Since our inception, we have incurred significant net losses. Our net loss was \$23.8 million for the year ended December 31, 2018. As of December 31, 2018, we had an accumulated deficit of \$122.9 million. We expect to continue to incur significant expenses and operating losses for the foreseeable future. Since inception, we have financed our operations with proceeds raised in our initial public offering and private placements of convertible debt and convertible preferred stock. We have no products approved for commercialization and have never generated any revenue from product sales.

We have devoted substantially all of our financial resources and efforts to the development of our clinical and preclinical product candidates and our proprietary half-life extending elastin-like polypeptide, or ELP, technology, including conducting preclinical studies and clinical trials. We recently completed a Phase 1 clinical trial of PB2452 and initiated a Phase 2b clinical trial of PB1046. We expect to continue to incur significant expenses and operating losses over the next several years. We expect that it could be several years, if ever, before we have a commercialized product. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially as we:

- continue our ongoing clinical trials of PB2452 and PB1046, as well as initiate and complete additional clinical trials, as needed;
- pursue regulatory approvals for PB2452 as a reversal agent for the antiplatelet drug ticagrelor and PB1046 for the treatment of pulmonary arterial hypertension, or PAH;
- seek to discover and develop additional clinical and preclinical product candidates;
- scale up our clinical and regulatory capabilities;
- establish a commercialization infrastructure and scale up external manufacturing and distribution capabilities to commercialize any product candidates for which we may obtain regulatory approval, including PB2452 and PB1046;

- adapt our regulatory compliance efforts to incorporate requirements applicable to marketed products;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, manufacturing and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and
- incur additional legal, accounting and other expenses in operating as a public company.

To become and remain profitable, we must succeed in developing and eventually commercializing product candidates that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, obtaining regulatory approval, and manufacturing, marketing and selling any product candidates for which we may obtain regulatory approval, as well as discovering and developing additional product candidates. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate any revenue or revenue that is significant enough to achieve profitability.

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

We have a limited operating history and no history of commercializing products, which may make it difficult for an investor to evaluate the success of our business to date and to assess our future viability.

We commenced operations in 2002, and our operations to date have been largely focused on raising capital and developing our clinical and preclinical product candidates and our proprietary ELP half-life extending technology, including undertaking preclinical studies and conducting clinical trials. To date, we have not yet demonstrated our ability to successfully complete later-stage clinical trials, obtain regulatory approvals, manufacture a product on a commercial scale, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing products.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We will need to transition at some point from a company with a development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We will need substantial additional funding to meet our financial obligations and to pursue our business objectives. If we are unable to raise capital when needed, we could be forced to curtail our planned operations and the pursuit of our growth strategy.

Our operations have consumed substantial amounts of cash since inception. 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 regulatory approval and achieve product sales. We expect to continue to incur significant expenses and operating losses over the next several years as we complete our ongoing clinical trials of our product candidates, initiate future clinical trials of our product candidates, seek marketing approval for PB2452 as a ticagrelor reversal agent and PB1046 for the treatment of PAH and advance any of our other product candidates we may develop or otherwise acquire. In addition, our product candidates, if approved, may not achieve commercial success. Our revenue, if any, will be derived from sales of products that we do not expect to be commercially available for a number of years, if at all. If we obtain marketing approval for PB2452, PB1046 or any other product candidates that we develop, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. We also expect an increase in our expenses associated with creating additional infrastructure to support operations as a public company.

In 2018, we received \$60.7 million in aggregate net proceeds from our initial public offering and the sale of our Series D convertible preferred stock. As of December 31, 2018, we had cash and cash equivalents of \$61.0 million. We believe that our existing cash and cash equivalents are sufficient to fund our operating expenses and capital requirements into the second quarter of 2020. This estimate is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we expect. Changes may occur beyond our control that would cause us to consume our available capital before that time, including changes in and progress of our development activities, acquisitions of additional product candidates, and changes in regulation. Our future capital requirements will depend on many factors, including:

- the progress and results of our ongoing and planned future clinical trials of PB2452 and PB1046 and our preclinical programs;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for any future product candidates we may decide to pursue;
- the extent to which we develop, in-license or acquire other product candidates and technologies;
- the number and development requirements of other product candidates that we may pursue;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- our ability to establish collaborations to commercialize PB1046 in the United States;
- our ability to establish collaborations to commercialize PB2452, PB1046 or any of our other product candidates outside the United States; and
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims.

We will require additional capital to commercialize PB2452 and PB1046. If we receive regulatory approval for either of these product candidates, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution, depending on where we choose to commercialize. Additional funds may not be available on a timely basis, on favorable terms, or at all, and such funds, if raised, may not be sufficient to enable us to continue to implement our long-term business strategy. If we are unable to raise sufficient additional capital, we could be forced to curtail our planned operations and the pursuit of our growth strategy.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial revenue, we may finance our cash needs through a combination of equity offerings, government or private party grants, debt financings and license and collaboration agreements. Aside from \$7.5 million of aggregate borrowings potentially available upon the achievement of certain milestones under our loan and security agreement with Silicon Valley Bank, or SVB, and WestRiver Innovation Lending Fund VIII, L.P. or WestRiver, we do not currently have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. For example, our loan and security agreement with SVB and WestRiver is secured by a first priority security interest in substantially all of our current and future assets, excluding intellectual property. We are also obligated to comply with various other customary covenants, including restrictions on our ability to encumber our intellectual property assets. The security interest granted to SVB and WestRiver may preclude future debt financing or make the terms of such financings less favorable.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Risks Related to the Development of Our Product Candidates

We have only two clinical-stage product candidates, PB2452, a ticagrelor reversal agent, and PB1046 for the treatment of PAH. If we are unable to successfully develop, receive regulatory approval for and commercialize our product candidates for these or any other indications, or successfully develop any other product candidates, or experience significant delays in doing so, our business will be harmed.

We currently have no products that are approved for commercial sale. We currently have only two clinical-stage product candidates, PB2452 and PB1046. To date, we have not yet conducted any later-stage clinical trials. We have not completed the development of any product candidates, and we may never be able to develop marketable products.

We have invested substantially all of our efforts and financial resources in the development of our clinical and preclinical product candidates and our proprietary ELP technology. Our ability to generate revenue from our product candidates, which we do not expect will occur for several years, if ever, will depend heavily on their successful development, regulatory approval and eventual commercialization of our product candidates. The success of PB2452, PB1046 or any other product candidates that we develop or otherwise may acquire will depend on several factors, including:

- timely and successful completion of preclinical studies and our clinical trials;
- sufficiency of our financial and other resources to complete the necessary preclinical studies and clinical trials;
- successful enrollment and completion of clinical trials;
- successful development of, or making arrangements with third-party manufacturers for, our commercial manufacturing processes for any of our product candidates that receive regulatory approval;
- receipt of timely marketing approvals from applicable regulatory authorities;
- launching commercial sales of products, if approved;
- acceptance of our products, if approved, by patients, the medical community and third-party payors, for their approved indications;
- the prevalence and severity of adverse events experienced with PB2452, PB1046 or any other product candidates;
- the availability, perceived advantages, cost, safety and efficacy of alternative therapies for any product candidate, and any indications for such product candidate, that we develop, specifically, alternative antiplatelet therapies to ticagrelor, including therapies that may be developed with a reversal agent, alternative reversal agents for ticagrelor or alternative treatments for PAH;
- our ability to produce PB2452, PB1046 or any other product candidates we develop on a commercial scale;
- obtaining and maintaining patent, trademark and trade secret protection and regulatory exclusivity for our product candidates and otherwise protecting our rights in our intellectual property portfolio;
- maintaining compliance with regulatory requirements, including current good manufacturing practices, or cGMPs;

- competing effectively with other procedures; and
- maintaining a continued acceptable safety, tolerability and efficacy profile of the products following approval.

If we are not successful with respect to one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize the product candidates we develop, which would materially harm our business. If we do not receive marketing approvals for PB2452, PB1046 or any other product candidate we develop, we may not be able to continue our operations.

The regulatory approval processes of the Food and Drug Administration, or FDA, and comparable foreign authorities are lengthy, time consuming and inherently unpredictable. If we are not able to obtain required regulatory approval for our product candidates, our business will be substantially harmed.

The time required to obtain approval or other marketing authorizations by the FDA and comparable foreign authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. PB2452 and PB1046 are currently our only clinical-stage product candidates. We have not obtained regulatory approval for any product candidate and it is possible that we may never obtain regulatory approval for PB2452, PB1046 or any product candidates we may seek to develop in the future. Neither we nor any future collaborator is permitted to market any drug product candidates in the United States until we receive regulatory approval of a biologics license application, or BLA, from the FDA. To date, we have only had limited discussions with the European Medicines Agency, or EMA, or other comparable foreign authorities regarding regulatory approval for PB2452, PB1046 or any other product candidate outside of the United States.

Prior to obtaining approval to commercialize any drug product candidate in the United States or abroad, we must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or foreign regulatory agencies, that such product candidates are safe, pure and effective for their intended uses. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. The FDA may also require us to conduct additional nonclinical studies or clinical trials for our product candidates either prior to or after approval, or it may object to elements of our clinical development programs.

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

We have invested a significant portion of our time and financial resources in the development of our clinical and preclinical product candidates, including PB2452 and PB1046. Our business is dependent on our ability to successfully complete preclinical and clinical development of, obtain regulatory approval for, and, if approved, successfully commercialize PB2452, PB1046 and any future product candidates in a timely manner.

Even if we eventually complete clinical testing and receive approval of a BLA or foreign marketing application for PB2452, PB1046 or any future product candidates, the FDA or the applicable foreign regulatory agency may grant approval or other marketing authorization contingent on the performance of costly additional clinical trials, including post-marketing clinical trials. The FDA or the applicable foreign regulatory agency also may approve or authorize for marketing a product candidate for a more limited indication or patient population than we originally request, and the FDA or applicable foreign regulatory agency may not approve or authorize the labeling that we believe is necessary or desirable for the successful commercialization of a product candidate. Any delay in obtaining, or inability to obtain, applicable regulatory approval or other marketing authorization would delay or prevent commercialization of that product candidate and would materially adversely impact our business and prospects.

In addition, the FDA and other regulatory authorities may change their policies, issue additional regulations or revise existing regulations, or take other actions, which may prevent or delay approval of our future products under development on a timely basis. Such policy or regulatory changes could impose additional requirements upon us that could delay our ability to obtain approvals, increase the costs of compliance or restrict our ability to maintain any marketing authorizations we may have obtained.

If considered appropriate by the FDA, we intend to seek regulatory approval of PB2452 in the United States through an accelerated approval process. If we are not successful with this process, the development or commercialization of PB2452 could be delayed, abandoned or significantly more costly.

The FDA's accelerated approval regulations allow drugs that are being developed to treat an unmet medical need to be approved substantially based on evidence of an effect on a surrogate biomarker endpoint that is considered reasonably likely to predict clinical benefit, rather than a clinical endpoint such as survival or irreversible morbidity. If considered appropriate by the FDA, our strategy is to use an accelerated approval pathway that would require that our Phase 3 clinical trial of PB2452 be ongoing at the time of BLA approval, and our BLA would be based on biomarker data from an initial subset of patients in this trial, together with safety data from our Phase 2 clinical trials. In such case, we expect that the FDA would require the completion of the Phase 3 clinical trial as a post-marketing commitment. We anticipate having an end-of-Phase 1 meeting with the FDA to discuss the regulatory pathway for PB2452. If the FDA requires the completion of the Phase 3 trial prior to the submission of a BLA, the development and commercialization timeline of PB2452 will be delayed. Further, the FDA may determine that the trials conducted by us were insufficient to support approval for all or some of the proposed indications, require us to conduct extensive post-approval studies or require us to make modifications to our ongoing Phase 3 clinical trial after approval and marketing.

Clinical product development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs and experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

In order to obtain FDA approval to market a new biological product we must demonstrate proof of safety, purity and efficacy in humans. The risk of failure for product candidates is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety, purity and potency, or efficacy, of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing or at any time during the trial process. The outcome of preclinical testing and early clinical trials may not be predictive of the results of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

We have not completed all clinical trials required for the approval of any of our product candidates. We cannot assure you that any clinical trial that we are conducting, or may conduct in the future, will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market our product candidates.

We may incur additional costs and experience delays in ongoing clinical trials for our product candidates, and we do not know whether future clinical trials, if any, will begin on time, need to be redesigned, enroll an adequate number of patients on time or be completed on schedule, if at all. We may experience numerous unforeseen events during or as a result of clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- 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 experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites or prospective contract research organizations, or CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- clinical trials of our product candidates may produce negative or inconclusive results, including failure to demonstrate statistical significance, and 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, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the trials;
- our third-party contractors 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 require that we or our investigators suspend or terminate clinical development for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate; and
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate.

If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not favorable or if there are safety concerns, 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 safety warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Success in preclinical studies or earlier clinical trials may not be indicative of results in future clinical trials.

Success in preclinical testing and early clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate. Preclinical tests and Phase 1 and Phase 2 clinical trials are primarily designed to test safety, to study pharmacokinetics and pharmacodynamics and to understand the side effects of product candidates at various doses and schedules. Success in preclinical or animal studies and early clinical trials does not ensure that later large-scale efficacy trials will be successful nor does it predict final results. Our product candidates may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies or having successfully advanced through initial clinical trials.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier-stage clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including changes in regulatory policy during the period of our product candidate development. Any such delays could negatively impact our business, financial condition, results of operations and prospects.

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

From time to time, we may publish interim top-line or preliminary results from our clinical trials. Interim results from clinical trials that we may complete are 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 results 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. Differences between preliminary or interim data and final data could significantly harm our business prospects and may cause the trading price of our common stock to fluctuate significantly.

Our clinical trials may fail to demonstrate the safety and efficacy of our product candidates, or serious adverse or unacceptable side effects may be identified during the development of our product candidates, which could prevent or delay regulatory approval and commercialization, increase our costs or necessitate the abandonment or limitation of the development of some of our product candidates.

Before obtaining regulatory approvals for the commercial sale of our product candidates, we must demonstrate through lengthy, complex and expensive preclinical testing and clinical trials that our product candidates are safe, pure and effective for use in each target indication, and failures can occur at any stage of testing. Clinical trials often fail to demonstrate safety or efficacy of the product candidate studied for the target indication.

If our product candidates are associated with side effects in clinical trials or have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow uses in which the side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. The FDA or an institutional review board may also require that we suspend, discontinue, or limit our clinical trials based on safety information, or that we conduct additional animal or human studies regarding the safety and efficacy of our product candidates which we have not planned or anticipated. Such findings could further result in regulatory authorities failing to provide marketing authorization for our product candidates or limiting the scope of the approved indication, if approved. Many product candidates that initially showed promise in early stage testing have later been found to cause side effects that prevented further development of the product candidate.

Additionally, if one or more of our product candidates receives marketing approval, and we or others identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the labels;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- we may not be able to achieve or maintain third-party payor coverage and adequate reimbursement; and
- our reputation and physician or patient acceptance of our products may suffer.

There can be no assurance that we will resolve any issues related to any product-related adverse events to the satisfaction of the FDA or foreign regulatory agency in a timely manner or at all. Moreover, any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations and prospects.

As an organization, we have never conducted pivotal clinical trials, and we may be unable to do so for any product candidates we may develop.

We will need to successfully complete pivotal clinical trials in order to obtain the approval of the FDA, EMA or other regulatory agencies to market PB2452, PB1046 or any future product candidate. Carrying out later-stage clinical trials is a complicated process. As an organization, we have not previously conducted any later stage or pivotal clinical trials. In order to do so, we will need to expand our clinical development and regulatory capabilities, and we may be unable to recruit and train qualified personnel. We also expect to continue to rely on third parties to conduct our pivotal clinical trials. See “— Risks Related to our Dependence on Third Parties —We will rely on third parties to conduct our future clinical trials for product candidates, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.” Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to BLA submission and approval of PB2452, PB1046 or future product candidates. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials, could prevent us from or delay us in commercializing our product candidates.

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

Successful and timely completion of clinical trials will require that we enroll a sufficient number of patients. Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors, including the size and nature of the patient population. Trials may be subject to delays as a result of patient enrollment taking longer than anticipated or patient withdrawal. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or foreign regulatory authorities. We cannot predict how successful we will be at enrolling subjects in future clinical trials. Subject enrollment is affected by other factors including:

- the eligibility criteria for the trial in question;
- the size of the patient population and process for identifying patients;
- the perceived risks and benefits of the product candidate in the trial;
- the availability of competing commercially available therapies and other competing drug candidates’ clinical trials;
- the willingness of patients to be enrolled in our clinical trials;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of patients for clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in these clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. Furthermore, we rely on and expect to continue to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials and we will have limited influence over their performance.

Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining enrollment of such patients in our clinical trials.

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

As product candidates proceed through preclinical studies to late-stage clinical trials towards potential approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and product characteristics. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the materials manufactured using altered processes. Such changes may also require additional testing, FDA notification or FDA approval. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commence sales and generate revenue.

Our clinical development of PB2452 depends on the continued use of ticagrelor as an antiplatelet therapy.

We are developing PB2452 as a ticagrelor reversal agent for the treatment of patients who are experiencing a major bleeding event or who require urgent surgery. If previously unknown safety risks related to ticagrelor are discovered that would affect its use as an antiplatelet therapy, we may pause or stop development of PB2452, which would significantly and adversely affect our business prospects.

ELP is a novel technology, which makes it difficult to predict the time, risks and cost of development and of subsequently obtaining regulatory approval of our ELP product candidates.

PB1046 and our preclinical product candidates are based on our proprietary ELP technology. Some of our future success depends on the successful development of this technology and products based on it. To our knowledge, no regulatory authority has granted approval to any person or entity, including us, to market and commercialize therapeutics using our novel ELP technology. We may never receive approval to market and commercialize any product candidate that utilizes ELP.

If we uncover any previously unknown risks related to our ELP technology, or if we experience unanticipated problems or delays in developing our ELP product candidates, we may be unable to complete our clinical trials and preclinical studies, meet the obligations of our license agreements or commercialize our product candidates on a timely or profitable basis. If serious adverse events or unacceptable side effects are observed in clinical trials or preclinical studies of a product candidate based on our ELP technology, our ability to develop other product candidates based on our ELP technology would be adversely affected.

We may not be able to obtain or maintain orphan drug designations or exclusivity for PB1046 or other product candidates, which could limit the potential profitability of such product candidates.

Regulatory authorities in some jurisdictions, including the United States, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States for which there is no reasonable expectation that the cost of developing and making available in the United States a drug or biologic for this type of disease or condition will be recovered from sales in the United States for that drug or biologic. Generally, a product that has orphan drug designation and subsequently receives the first FDA approval for the disease for which it has such designation is entitled to orphan drug exclusive approval (or exclusivity), which means that the FDA may not approve any other applications, including a full BLA, to market the same drug or biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation.

The FDA has granted two orphan drug designations for PB1046, one for the treatment of PAH and a second for cardiomyopathy associated with DMD. We may seek orphan drug designation for future indications for PB1046 or for other product candidates. Even if we were to obtain orphan drug designation for a product candidate, we may not obtain orphan exclusivity and that exclusivity may not effectively protect the drug from the competition of different drugs for the same condition, which could be approved during the exclusivity period. Additionally, after an orphan drug is approved, the FDA could subsequently approve another application for the same drug for the same indication if the FDA concludes that the later drug is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusive marketing rights in the United States also may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. The failure to obtain an orphan drug designation for any product candidates we may develop, the inability to maintain that designation for the duration of the applicable period, or the inability to obtain or maintain orphan drug exclusivity could reduce our ability to make sufficient sales of the applicable product candidate to balance our expenses incurred to develop it, which would have a negative impact on our operational results and financial condition.

A breakthrough therapy designation by the FDA for a product candidate may not lead to a faster development or regulatory review or approval process, and it would not increase the likelihood that the product candidate will receive marketing approval.

We may seek a breakthrough therapy designation for one or more product candidates. A breakthrough therapy is defined as a product candidate that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product candidate 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 product candidates that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Product candidates designated as breakthrough therapies by the FDA are also eligible for priority review if supported by clinical data at the time of the submission of the BLA.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to product candidates considered for approval under conventional FDA procedures and it would not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the product candidate no longer meets the conditions for qualification or it may decide that the time period for FDA review or approval will not be shortened.

We may not be successful in our efforts to increase our pipeline of product candidates, including by pursuing additional indications for our current product candidate or in-licensing or acquiring additional product candidates for other orphan diseases.

A key element of our strategy is to build and expand our pipeline of product candidates, including by developing PB1046 for the treatment of other orphan conditions and identifying other product candidates using our ELP technology. In addition, we may in-license or acquire additional product candidates for other orphan diseases. We may not be able to identify or develop product candidates that are safe, tolerable and effective. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify, in-license or acquire may not be suitable for clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance.

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

Because we have limited financial and management resources, we focus on development programs and product candidates that we identify for specific indications. As such, we are currently primarily focused on the development of PB2452 as a ticagrelor reversal agent and PB1046 for the treatment of PAH. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications for PB1046 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 development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

Risks Related to the Commercialization of Our Product Candidates

Market acceptance of PB2452, if approved, will depend heavily on the continued market acceptance and use of ticagrelor.

The commercial success of PB2452 as a ticagrelor reversal agent, if approved, is dependent on the continued market acceptance and use of ticagrelor as an antiplatelet therapy. Ticagrelor competes against other commercially available antiplatelet therapies, including other P2Y₁₂ receptor antagonists, many of which are available as generic drugs and therefore significantly less expensive than ticagrelor. New antiplatelet therapies may also be developed in the future, including other P2Y₁₂ receptor antagonists and other antiplatelet therapies, which could also have reversal agents, that could displace ticagrelor as the American College of Cardiology, American Heart Association and European Society of Cardiology's preferred antiplatelet agent for acute coronary syndrome or otherwise reduce ticagrelor's market position. Any such changes in the market acceptance and use of ticagrelor would significantly harm our business, results of operations and prospects for PB2452.

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

If any of our product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant revenue and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy, safety and potential advantages compared to alternative treatments;
- our ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- product labeling or product insert requirements of the FDA or foreign regulatory authorities, including any limitations or warnings contained in a product's approved labeling, including any black box warning;
- the willingness of the target patient population to try new treatments and of physicians to prescribe these treatments;
- our ability to hire and retain a sales force in the United States;
- the strength of marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement for PB2452, PB1046 and any other product candidates, once approved;

- the prevalence and severity of any side effects; and
- any restrictions on the use of our products together with other medications.

If we are unable to establish sales, marketing and distribution capabilities for PB2452, PB1046 or any other product candidate that may receive regulatory approval, we may not be successful in commercializing those product candidates if and when they are approved.

We do not have sales or marketing infrastructure. To achieve commercial success for PB2452, PB1046 and any other product candidate for which we may obtain marketing approval, we will need to establish a sales and marketing organization. In the future, we expect to build a focused sales and marketing infrastructure to market some of our product candidates in the United States, if and when they are approved. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to market our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians in order to educate physicians about our product candidates, once approved;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable to establish our own sales, marketing and distribution capabilities and are forced to enter into arrangements with, and rely on, third parties to perform these services, our revenue and our profitability, if any, are likely to be lower than if we had developed such capabilities ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

We face substantial competition, which may result in a smaller than expected commercial opportunity and/or others discovering, developing or commercializing products before or more successfully than we do.

The life sciences industry is highly competitive. 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 many different sources, including major pharmaceutical and specialty pharmaceutical companies, compounding facilities, academic institutions and governmental agencies and public and private research institutions.

Although there are currently no known reversal agents approved or in clinical development for ticagrelor, there can be no assurance that competitors will not seek to develop a competing product. Moreover, the success of PB2452, if approved, will be dependent on the continued success of ticagrelor. See “—Market acceptance of PB2452, if approved, will depend heavily on the continued market acceptance and use of ticagrelor.”

We are aware of several other products and product candidates as potential treatments for PAH that would compete with PB1046. Although we anticipate that PB1046 may be used as a complement to patients' existing therapies, we expect to compete with existing treatments for PAH patients with Class II-IV symptoms that target the endothelin, nitric oxide and prostacyclin pathways, as well as any generic equivalents that may be developed, particularly generic equivalents of Tyvaso following the expiry of its patent protection in 2018. In addition to currently approved drugs within these classes, we are also aware of a number of PAH therapies in clinical development with which PB1046 would compete if approved.

In addition, our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than PB2452, PB1046 or any other product 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 our product, which could result in our competitors establishing a strong market position before we are able to enter the market.

Many of the companies against which we are competing, or against which we may compete in the future, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved 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. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or that may be necessary for, our programs.

The success of PB2452 as a ticagrelor reversal agent and PB1046 for the treatment of PAH, or any future product candidate, will depend significantly on coverage and adequate reimbursement or the willingness of patients to pay for these procedures.

We believe our success depends on obtaining and maintaining coverage and adequate reimbursement for PB2452 as a ticagrelor reversal agent and PB1046 for the treatment of PAH and/or procedures utilizing PB2452, PB1046 or any other product candidate, and the extent to which patients will be willing to pay out of pocket for such products and procedures, in the absence of reimbursement for all or part of the cost. Obtaining coverage and adequate reimbursement for our products may be particularly difficult because of the higher prices often associated with drugs administered under the supervision of a physician. Separate reimbursement for the product itself or the treatment or procedure in which our product is used may not be available. Even if the procedure using our product is covered, third-party payors, such as Medicare, Medicaid, managed care organizations, and private health insurers, may package the cost of the drug into the procedure payment and not separately reimburse the physician for the costs associated with our product. A decision by a third-party payor not to cover or separately reimburse for our products could reduce physician utilization of our products once approved. Additionally, in the United States, there is no uniform policy of coverage and reimbursement among third-party payors. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. However, decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a payor-by-payor basis. One payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage, and adequate reimbursement.

Third-party payors determine which products and procedures they will cover and establish reimbursement levels. Even if a third-party payor covers a particular product or procedure, the resulting reimbursement payment rates may not be adequate. Patients who are treated in-office for a medical condition generally rely on third-party payors to reimburse all or part of the costs associated with the procedure, including costs associated with products used during the procedure, and may be unwilling to undergo such procedures in the absence of such coverage and adequate reimbursement. Physicians may be unlikely to offer procedures for such treatment if they are not covered by insurance and may be unlikely to purchase and use our product candidates, if approved, for our stated indications unless coverage is provided and reimbursement is adequate.

Reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that a procedure is safe, effective and medically necessary; appropriate for the specific patient; cost-effective; supported by peer-reviewed medical journals; included in clinical practice guidelines; and neither cosmetic, experimental, nor investigational.

Further, from time to time, typically on an annual basis, payment rates are updated and revised by third-party payors. An example of payment updates is the Medicare program updates to physician payments, which is done on an annual basis. In the past, when the application of the formula resulted in lower payment, Congress has passed interim legislation to prevent the reductions. The Medicare Access and CHIP Reauthorization Act of 2015, or MACRA, ended the use of the statutory formula and provided for a 0.5% annual increase in payment rates under the Medicare Physician Fee Schedule through 2019, but no annual update from 2020 through 2025. MACRA also introduced a merit-based incentive bonus program for Medicare physicians beginning in 2019. At this time, it is unclear how the introduction of the merit-based incentive program will impact overall physician reimbursement under the Medicare program. Any resulting decrease in payment under the merit-based reimbursement system may adversely affect our revenue and results of operations. In addition, the Medicare physician fee schedule has been adapted by some private payors into their plan-specific physician payment schedule. We cannot predict how pending and future healthcare legislation will impact our business, and any changes in coverage and reimbursement that further restricts coverage of our product candidates or lowers reimbursement for procedures using our products could harm our business.

Foreign governments also have their own healthcare reimbursement systems, which vary significantly by country and region, and we cannot be sure that coverage and adequate reimbursement will be made available with respect to the treatments in which our products are used under any foreign reimbursement system.

There can be no assurance that PB2452, PB1046 or any other product candidate, if approved for sale in the United States or in other countries, will be considered medically reasonable and necessary, that it will be considered cost-effective by third-party payors, that coverage or an adequate level of reimbursement will be available or that reimbursement policies and practices in the United States and in foreign countries where our products are sold will not adversely affect our ability to sell our product candidates profitably, if they are approved for sale.

The market for PB2452, PB1046 and any other product candidates may be smaller than we expect.

Our estimates of the potential market opportunity for PB2452, PB1046 and any other product candidates include several key assumptions based on our industry knowledge, industry publications and third-party research reports. These assumptions include, for PB2452, the number of patients on ticagrelor who will experience major bleeding or who will require urgent surgery, and for PB1046, the number of patients with PAH, as well as the estimated reimbursement levels for each product candidate if approved. However, there can be no assurance that any of these assumptions are, or will remain, accurate. If the actual market for PB2452 or PB1046 or for any other product candidate we may develop is smaller than we expect, our revenues, if any, may be limited and it may be more difficult for us to achieve or maintain profitability.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or drugs caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or drugs that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards paid to trial participants or patients;

- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

We currently hold \$5,000,000 in product liability insurance coverage in the aggregate, with a per incident limit of \$5,000,000, which may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Our business and operations would suffer in the event of computer system failures, cyberattacks or a deficiency in our cybersecurity.

Despite the implementation of security measures, our internal computer systems, and those of third parties on which we rely, are vulnerable to damage from computer viruses, malware, natural disasters, terrorism, war, telecommunication and electrical failures, cyberattacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization. The risk of a security breach or disruption, particularly through cyberattacks or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product development programs. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach was to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur material legal claims and liability, damage to our reputation, and the further development of our product candidates could be delayed.

Risks Related to Our Dependence on Third Parties

We will rely on third parties to conduct our future clinical trials for product candidates, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We do not independently conduct the clinical trials for any of our product candidates. We have engaged CROs to conduct our ongoing clinical trial of PB2452 and to assist in conducting portions of our ongoing clinical trial of PB1046. We expect to engage CROs for future clinical trials for PB2452, PB1046 or other product candidates that we may progress to clinical development. We expect to continue to rely on third parties, including clinical data management organizations, medical institutions and clinical investigators, to conduct those clinical trials. Any of these third parties may terminate their engagements with us, some in the event of an uncured material breach and some at any time for convenience. If any of our relationships with these third parties terminate, we may not be able to timely enter into arrangements with alternative third parties or to do so on commercially reasonable terms, if at all. Switching or adding CROs involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we intend to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

In addition, any third parties conducting our clinical trials will not be our employees, and except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our clinical programs. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. Consequently, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase substantially and our ability to generate revenue could be delayed significantly.

We rely on these parties for execution of our preclinical studies and clinical trials, and generally do not control their activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as good clinical practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. If we or any of our CROs or other third parties, including trial sites, fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP conditions. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA. The FDA may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the trial. The FDA may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA and may ultimately lead to the denial of marketing approval of PB2452, PB1046 and any other product candidates.

We also expect to rely on other third parties to store and distribute product supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential revenue.

We contract with third parties for the manufacture of PB2452 and PB1046 for clinical drug supply and expect to continue to do so for commercialization if approved. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not have any cGMP manufacturing facilities. We currently rely, and expect to continue to rely, on third parties for the cGMP manufacture of PB2452, PB1046 or any other product candidates which we may pursue, for clinical development as well as for commercial manufacture of PB2452, PB1046 or any other product candidate which we may pursue if we receive marketing approval. We also rely on a proprietary *E. coli* strain owned by Wacker Biotech GmbH, or Wacker, for the production of PB2452. Our reliance on Wacker's *E. coli* strain increases the risk that we will not have sufficient quantities of PB2452 or be able to obtain quantities at an acceptable cost or quality, which could delay, prevent or impair our ability to timely conduct our clinical trials or our other development or commercialization efforts. We will continue to rely on Wacker to manufacture our clinical supply of PB2452 for our planned Phase 2a and Phase 2b clinical trials. We recently engaged BioVectra, Inc., another cGMP manufacturing facility, for the later-stage clinical and commercial production of PB2452, if approved.

With respect to PB2452, we filled and released PB2452 drug substance, manufactured by Wacker and provided to us pursuant to our license agreement, for our Phase 1 clinical trial. As we scale our manufacturing of PB2452 to meet potential commercial demand, if PB2452 is approved, we have initiated a technology transfer of our current manufacturing process of PB2452 to BioVectra. Although we expect that we will have sufficient manufacturing capacity from Wacker for our planned Phase 2a and Phase 2b clinical trials, we expect to use BioVectra to manufacture our later-stage clinical and commercial supply of PB2452, if approved. We will need to perform analytical and other tests to demonstrate that the new materials produced by Wacker, BioVectra, or any other future third-party manufacturer that we engage, are comparable in all respects to the product utilized in our Phase 1 clinical trial. There is no assurance that any such product will pass the required comparability testing, that

any other future third-party manufacturer that we engage will be successful in producing PB2452 or that any materials produced by Wacker, BioVectra or any other third-party manufacturer that we engage will have the same effect in patients that we have observed to date with respect to materials used in our Phase 1 clinical trial. Moreover, if supplies are interrupted or result in poor yield or quality, it would materially harm our business. BioVectra will be required to scale up its manufacturing process to meet our future needs of PB2452 for later-stage clinical development and, if approved, commercialization. If BioVectra is unable to successfully scale up the manufacturing process, we would need to find alternative manufacturing facilities or an alternative manufacturing process, which we may not be able to do on a timely basis or on commercially reasonable terms, if at all, and which could adversely affect the clinical development of PB2452.

We also expect to rely on third-party manufacturers or third-party collaborators for the manufacture of commercial supply of PB2452, PB1046 or any other product candidates for which we obtain marketing approval. The facilities used by our contract manufacturers to manufacture our product candidates must be inspected by the FDA or other regulatory authorities after we submit our BLA or comparable marketing application to the FDA or other regulatory authority. We do not have control over a supplier's or manufacturer's compliance with laws, regulations and applicable cGMP standards or similar regulatory requirements and other laws and regulations, such as those related to environmental health and safety matters. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, we may be unable to obtain regulatory approval of our marketing applications. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority finds deficiencies with or does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

We may be unable to establish any agreements with future third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, qualifying and validating such manufacturers may take a significant period of time and reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the incurrence of upfront scale-up costs prior to commercial approval;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how;
- the possible increase in costs for the raw materials for our product candidates; and
- the possible termination or nonrenewal of any agreement by any third party at a time that is costly or inconvenient for us.

Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

Our product candidates, and any drugs that we may develop, may compete with other product candidates and drugs for access to manufacturing facilities. There are no assurances we would be able to enter into similar commercial arrangements with other manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us in a timely manner. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval.

We may seek collaborations with third parties for the development or commercialization of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

We may seek third-party collaborators for the development and commercialization of our product candidates, including for the commercialization of any of our product candidates that are approved for marketing outside the United States. Our likely collaborators for any collaboration arrangements include regional and national pharmaceutical companies and biotechnology companies. If we do enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenue from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates would pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for 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;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or drugs, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such 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 or their intellectual property rights or may use our or their proprietary information in such a way as to invite litigation that could jeopardize or invalidate such 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 for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

We may seek to establish collaborations, and if we are unable to do so, we may have to alter our development and commercialization plans.

Our product development programs and the potential commercialization of our product candidates will require substantial additional capital. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those 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 design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of such product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate revenue.

Risks Related to Our Intellectual Property

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

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our product candidates and our ELP technology. Our success depends in large part on our ability to obtain and maintain patent and other intellectual property protection in the United States and in other countries with respect to our proprietary technology and product candidates.

As of the date of this Annual Report on Form 10-K, our patent estate contained at least 15 patent families that we own or in-license that protect various aspects of our product candidates or our ELP technology platform. We own or have rights in 20 United States patents, over 10 United States patent applications, over 50 foreign patents and over 40 foreign patent applications. We cannot offer any assurances about which of our patent applications will issue, the breadth of any resulting patent or whether any of the issued patents will be found invalid and unenforceable or will be threatened by third parties. We cannot offer any assurances that the breadth of our granted patents will be sufficient to stop a competitor from developing and commercializing a product, including a biosimilar product that would be competitive with one or more of our product candidates. Furthermore, any successful challenge to these patents or any other patents owned by or licensed to us after patent issuance could deprive us of rights necessary for the successful commercialization of any of our product candidates. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

The patent prosecution process is expensive and time-consuming. We may not be able to prepare, file and prosecute all necessary or desirable patent applications for a commercially reasonable cost or in a timely manner or in all jurisdictions. It is also possible that we may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Moreover, depending on the terms of any future in-licenses to which we may become a party, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology in-licensed from third parties. Therefore, these patents and patent applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

In addition to the protection provided by our patent estate, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not amenable to patent protection. Although we generally require all of our employees to assign their inventions to us, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information, or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed, or that our trade secrets and other confidential proprietary information will not be disclosed. Moreover, our competitors may independently develop knowledge, methods and know-how equivalent to our trade secrets. Competitors could purchase our products, if approved, and replicate some or all of the competitive advantages we derive from our development efforts for technologies on which we do not have patent protection. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, our agreements or security measures may be breached, and we may not have adequate remedies for any breach. Also, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA is considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future. If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

Patent terms may be inadequate to protect our competitive position on our products for an adequate amount of time, and if we do not obtain protection under the Hatch-Waxman Amendments and similar non-U.S. legislation for extending the term of patents covering each of our product candidates, our business may be materially harmed.

Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments, and similar legislation in the European Union. The Hatch-Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent may be extended, and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be reduced and could have a material adverse effect on our business.

If we fail to comply with our obligations in our current and future intellectual property licenses and funding arrangements with third parties, we could lose rights that are important to our business.

We are heavily reliant upon licenses to certain patent rights and proprietary technology for the development of PB2452, PB1046 and our ELP technology. These license agreements impose diligence, development and commercialization timelines and milestone payment, royalty, insurance and other obligations on us. If we fail to comply with our obligations, our licensors may have the right to terminate our licenses, in which event we might not be able to develop, manufacture or market any product that is covered by the intellectual property we in-license from such licensor and may face other penalties. Such an occurrence would materially adversely affect our business prospects.

Licenses to additional third-party technology and materials that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms, or at all, which could have a material adverse effect on our business and financial condition. Although we control the prosecution, maintenance and enforcement of the licensed and sublicensed intellectual property relating to PB2452, we may require the cooperation of our licensor and any upstream licensors, which may not be forthcoming. Therefore, we cannot be certain that the prosecution, maintenance and enforcement of these patent rights will be in a manner consistent with the best interests of our business. If we or our licensor fail to maintain such patents, or if we or our licensor lose rights to those patents or patent applications, 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 will also apply to patent rights we may own in the future. Further, if we fail to comply with our development obligations under our license agreements, we may lose our patent rights with respect to such agreement on a territory-by-territory basis, which would affect our patent rights worldwide.

Termination of our current or any future license agreements would reduce or eliminate our rights under these agreements and may result in our having to negotiate new or reinstated agreements with less favorable terms or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology. Any of the foregoing could prevent us from commercializing our other product candidates, which could have a material adverse effect on our operating results and overall financial condition.

In addition, intellectual property rights that we in-license in the future may be sublicenses under intellectual property owned by third parties, in some cases through multiple tiers. The actions of our licensors may therefore affect our rights to use our sublicensed intellectual property, even if we are in compliance with all of the obligations under our license agreements. Should our licensors or any of the upstream licensors fail to comply with their obligations under the agreements pursuant to which they obtain the rights that are sublicensed to us, or should such agreements be terminated or amended, our ability to develop and commercialize our product candidates may be materially harmed.

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our future patents.

Our ability to obtain patents is highly uncertain because, to date, some legal principles remain unresolved, and there has not been a consistent policy regarding the breadth or interpretation of claims allowed in patents in the United States. Furthermore, the specific content of patents and patent applications that are necessary to support and interpret patent claims is highly uncertain due to the complex nature of the relevant legal, scientific, and factual issues. Changes in either patent laws or interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property or narrow the scope of our patent protection.

For example, on September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act included a number of significant changes to United States patent law. These included provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The United States Patent and Trademark Office, or USPTO, has developed new and untested regulations and procedures to govern the full implementation 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, became effective in March 2013. The Leahy-Smith Act has also introduced procedures making it easier for third parties to challenge issued patents, as well as to intervene in the prosecution of patent applications. Finally, the Leahy-Smith Act contained new

statutory provisions that require the USPTO to issue new regulations for their implementation, and it may take the courts years to interpret the provisions of the new statute. It is too early to tell what, if any, impact the Leahy-Smith Act will have on the operation of our business and the protection and enforcement of our intellectual property. 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 future patents. Further, the U.S. 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 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 actions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce patents that we have owned or licensed or that we might obtain in the future. An inability to obtain, enforce, and defend patents covering our proprietary technologies would materially and adversely affect our business prospects and financial condition.

Similarly, changes in patent laws and regulations in other countries or jurisdictions, changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we may obtain in the future. Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. For example, if the issuance in a given country of a patent covering an invention is not followed by the issuance in other countries of patents covering the same invention, or if any judicial interpretation of the validity, enforceability or scope of the claims or the written description or enablement, in a patent issued in one country is not similar to the interpretation given to the corresponding patent issued in another country, our ability to protect our intellectual property in those countries may be limited. Changes in either patent laws or in interpretations of patent laws in the United States and other countries may materially diminish the value of our intellectual property or narrow the scope of our patent protection.

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

Competitors may infringe the patents we have applied for. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. If we initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product or product candidate is invalid and/or unenforceable. In patent litigation in the United States, counterclaims alleging invalidity and/or unenforceability are common, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. In an infringement proceeding, a court may decide that the patent claims we are asserting are invalid and/or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patent claims do not cover the technology in question. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review, *inter partes* review and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in revocation of or amendment to our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we, our patent counsel, and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing and could have a material adverse impact on our business.

Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patent applications. An unfavorable outcome could require us to cease using the related technology or force us to take a license under the patent rights of the prevailing party, if available. Furthermore, our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. 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 our common stock.

We may be unsuccessful in licensing or acquiring intellectual property from third parties that may be required to develop and commercialize our product candidates.

A third party may hold intellectual property, including patent rights that are important or necessary to the development and commercialization of our product candidates. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our product candidates, in which case we would be required to acquire or obtain a license to such intellectual property from these third parties, and we may be unable to do so on commercially reasonable terms or at all. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business.

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

As our current and future product candidates progress toward commercialization, the possibility of a patent infringement claim against us increases. We cannot provide any assurance that our current and future product candidates do not infringe other parties' patents or other proprietary rights, and competitors or other parties may assert that we infringe their proprietary rights in any event. We may become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our current and future product candidates, including interference or derivation proceedings before the USPTO. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could have a negative impact on our ability to commercialize PB2452, PB1046 and any future product candidates. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is high and requires us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would agree with us and invalidate the claims of any such U.S. patent. Moreover, given the vast number of patents in our field of technology, we cannot be certain that we do not infringe existing patents or that we will not infringe patents that may be granted in the future.

While we may decide to initiate proceedings to challenge the validity of these or other patents in the future, we may be unsuccessful, and courts or patent offices in the United States and abroad could uphold the validity of any such patent. Furthermore, because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of our product candidates. Regardless of when filed, we may fail to identify relevant third-party patents or patent applications, or we may incorrectly conclude that a third-party patent is invalid or not infringed by our product candidates or activities. If a patent holder believes that one of our product candidates infringes its patent, the patent holder may sue us even if we have received patent protection for our technology. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant drug revenue and against whom our own patent portfolio may thus have no deterrent effect. If a patent infringement suit were threatened or brought against us, we could be forced to stop or delay research, development, manufacturing or sales of the drug or product candidate that is the subject of the actual or threatened suit.

If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue commercializing our product candidates. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if a license can be obtained on acceptable terms, the rights may be non-exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. If we fail to obtain a required license, we may be unable to effectively market product candidates based on our technology, which could limit our ability to generate revenue or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. Alternatively, we may need to redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. Under certain circumstances, we could be forced, including by court orders, to cease commercializing our product candidates. In addition, in any such proceeding or litigation, we could be found liable for substantial monetary damages, potentially including treble damages and attorneys' fees, if we are found to have willfully infringed the patent at issue. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could harm our business. Any claims by third parties that we have misappropriated their confidential information or trade secrets could have a similar negative impact on our business.

The cost to us in defending or initiating any litigation or other proceeding relating to patent or other proprietary rights, even if resolved in our favor, could be substantial, and litigation would divert our management's attention. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and limit our ability to continue our operations.

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

We employ individuals who were previously employed at other biotechnology or biopharmaceutical companies. Although we try to ensure that our employees, consultants and advisors 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 our employees, consultants, or independent contractors have inadvertently or otherwise used or disclosed confidential information of our employees' former employers or other third parties. We may also be subject to claims that former employers or other third parties have an ownership interest in our future patents. Litigation may be necessary to defend against these claims. There is no guarantee of success in defending these claims, and even if we are successful, litigation could result in substantial cost and be a distraction to our management and other employees.

We may be subject to claims challenging the inventorship or ownership of our future patents and other intellectual property.

We may also be subject to claims that former employees, collaborators, or other third parties have an ownership interest in our patent applications, our future patents, or other intellectual property. We may be subject to ownership disputes in the future arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates. Although it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own, and we cannot be certain that our agreements with such parties will be upheld in the face of a potential challenge, or that they will not be breached, for which we may not have an adequate remedy. The assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

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

If we rely on third parties to manufacture or commercialize PB2452, PB1046 or any future product candidates, or if we collaborate with additional third parties for the development of PB2452, PB1046 or any future product candidates, we must, at times, share trade secrets with them. We may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure could have an adverse effect on our business and results of operations.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets. Despite our efforts to protect our trade secrets, we may not be able to prevent the unauthorized disclosure or use of our technical know-how or other trade secrets by the parties to these agreements. Moreover, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our confidential information or proprietary technology and processes. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the collaborators, scientific advisors, employees, contractors and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a result. Moreover, if confidential information that is licensed or disclosed to us by our partners, collaborators, or others is inadvertently disclosed or subject to a breach or violation, we may be exposed to liability to the owner of that confidential information. Enforcing a claim that a third party illegally obtained and is using our trade secrets, like patent litigation, is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets.

We may enjoy only limited geographical protection with respect to certain patents and we may not be able to protect our intellectual property rights throughout the world.

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

In addition, we may decide to abandon national and regional patent applications before they are granted. The examination of each national or regional patent application is an independent proceeding. As a result, patent applications in the same family may issue as patents in some jurisdictions, such as in the United States, but may issue as patents with claims of different scope or may even be refused in other jurisdictions. It is also quite common that depending on the country, the scope of patent protection may vary for the same product candidate or technology.

While we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets. If we encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished, and we may face additional competition from others in those jurisdictions.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws or rules and regulations in the United States and Europe, and many companies have encountered significant difficulties in protecting and defending such rights in such jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property rights, which could make it difficult for us to stop the infringement of our future patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in other jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our future patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing as patents, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Some countries also have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In those countries, the patent owner may have limited remedies, which could materially diminish the value of such patents. If we are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired.

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

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and/or applications will be due to be paid to the USPTO and various government patent agencies outside of the United States over the lifetime of our patents and/or applications and any patent rights we may obtain in the future. Furthermore, the USPTO and various non-U.S. government patent agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. In many cases, an inadvertent lapse of a patent or patent application can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment or lapse of the patents or patent applications, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market, which could have a material adverse effect on our business.

Any trademarks we have obtained or may obtain may be infringed or otherwise violated, or successfully challenged, resulting in harm to our business.

We expect to rely on trademarks as one means to distinguish our product candidates, if approved for marketing, from the drugs of our competitors. Once we select new trademarks and apply to register them, our trademark applications may not be approved. Third parties may oppose or attempt to cancel our trademark applications or trademarks, or otherwise challenge our use of the trademarks. In the event that our trademarks are successfully challenged, we could be forced to rebrand our drugs, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe or otherwise violate our trademarks and we may not have adequate resources to enforce our trademarks. Any of the foregoing events may have a material adverse effect on our business.

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

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

- others may be able to make products that are similar to or otherwise competitive with our product candidates but that are not covered by the claims of our current or future patents;

- an in-license necessary for the manufacture, use, sale, offer for sale or importation of one or more of our product candidates may be terminated by the licensor;
- we or future collaborators might not have been the first to make the inventions covered by our issued or future issued patents or our pending patent applications;
- we or future collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or in-license may be held invalid or unenforceable as a result of legal challenges by our competitors;
- issued patents that we own or in-license may not provide coverage for all aspects of our product candidates in all countries;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

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

Risks Related to Legal and Regulatory Compliance Matters

Our relationships with customers, healthcare providers, physicians and third-party payors are subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

Healthcare providers, physicians and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers and third-party payors subject us to various federal and state fraud and abuse laws and other healthcare laws, including, without limitation, the federal Anti-Kickback Statute, the federal civil and criminal false claims laws and the law commonly referred to as the Physician Payments Sunshine Act and regulations promulgated under such laws. These laws will impact, among other things, our clinical research, proposed sales, marketing and educational programs, and other interactions with healthcare professionals. In addition, we may be subject to patient privacy laws by both the federal government and the states in which we conduct or may conduct our business. The laws that will affect our operations include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, individuals or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind in return for, or to induce, either the referral of an individual, or the purchase, lease, order or arrangement for or recommendation of the purchase, lease, order or arrangement for any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. The term “remuneration” has been broadly interpreted to include anything of value. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe

harbor. A person does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, signed into law in 2010, provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act;

- the federal civil and criminal false claims laws, including, without limitation, the federal False Claims Act, which can be enforced by private citizens through civil whistleblower or qui tam actions, and civil monetary penalty laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from the federal government, including Medicare, Medicaid and other government payors, that are false or fraudulent or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim or to avoid, decrease or conceal an obligation to pay money to the federal government. A claim includes “any request or demand” for money or property presented to the U.S. federal government. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies’ marketing of products for unapproved, and thus non-reimbursable, uses;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes which prohibit, among other things, a person from knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. 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 it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information on health plans, healthcare clearinghouses and certain healthcare providers, known as “covered entities”, and their respective HIPAA “business associates”, independent contractors that perform certain services involving the use or disclosure of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorneys’ fees and costs associated with pursuing federal civil actions;
- the federal transparency laws, including the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, medical devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the State Children’s Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to: (1) payments or other “transfers of value” made to physicians and teaching hospitals, and (2) ownership and investment interests held by physicians and their immediate family members; and
- state and foreign law equivalents of each of the above federal laws and regulations; state laws that require manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; state laws that require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or that otherwise restrict payments that may be made to healthcare providers; state and local laws that require the registration of pharmaceutical sales representatives; and state and foreign laws that 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.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. 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 regulations that may apply to us, we may be subject to significant penalties, including, without limitation, civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from participating in federal and state funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, diminished profits and future earnings, reputational harm and the curtailment or restructuring of our operations, any of which could harm our business.

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. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance and/or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

Even if we obtain regulatory approval for PB2452, PB1046 or any future product candidates, they will remain subject to ongoing regulatory oversight.

Even if we obtain any regulatory approval for PB2452, PB1046 or any future product candidates, such product candidates, once approved, will be subject to ongoing regulatory requirements applicable to manufacturing, labeling, packaging, storage, advertising, promoting, sampling, record-keeping and submitting of safety and other post-market information, among other things. Any regulatory approvals that we receive for PB2452, PB1046 or any future product candidates may also be subject to a risk evaluation and mitigation strategy, limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or requirements that we conduct potentially costly post-marketing testing, including Phase 4 trials, and in the event that we receive accelerated approval of PB2452, the completion of a Phase 3 trial, and surveillance to monitor the quality, safety and efficacy of the drug. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval. We will further be required to immediately report any serious and unexpected adverse events and certain quality or production problems with our products to regulatory authorities along with other periodic reports.

Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. We will also have to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drug products are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we will not be allowed to promote our products for indications or uses for which they do not have approval, commonly known as off-label promotion. The holder of an approved BLA must submit new or supplemental applications and obtain prior approval for certain changes to the approved product, product labeling, or manufacturing process.

In addition, drug manufacturers are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements and adherence to commitments made in the BLA or foreign marketing application. If we, or a regulatory authority, discover previously unknown problems with a drug, such as adverse events of unanticipated severity or frequency, or problems with the facility where the drug is manufactured or if a regulatory authority disagrees with the promotion, marketing or labeling of that drug, a regulatory authority may impose restrictions relative to that drug, the manufacturing facility or us, including requesting a recall or requiring withdrawal of the drug from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements following approval of PB2452, PB1046 or any future product candidates, a regulatory authority may:

- issue an untitled letter or warning letter asserting that we are in violation of the law;
- seek an injunction or impose administrative, civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending BLA or comparable foreign marketing application (or any supplements thereto) submitted by us or our strategic partners;
- restrict the marketing or manufacturing of the drug;
- seize or detain the drug or otherwise require the withdrawal of the drug from the market;
- refuse to permit the import or export of product candidates; or
- refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize PB2452, PB1046 or any future product candidates and harm our business, financial condition, results of operations and prospects.

Healthcare legislative or regulatory reform measures may have a negative impact on our business and results of operations.

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. In March 2010, the ACA was passed, which substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry. The ACA, among other things: (1) established an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs; (2) expanded the entities eligible for discounts under the 340B drug pricing program; (3) increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively and capped the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price, or AMP; (4) expanded the eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability; (5) addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for certain drugs and biologics that are inhaled, infused, instilled, implanted or injected; (6) introduced a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; (7) created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and (8) established a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug.

Some of the provisions of the ACA have yet to be implemented, and there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the ACA. While Congress has not passed comprehensive repeal legislation, bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act of 2017, or Tax Act, includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate.” On January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called “Cadillac” tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. The Bipartisan Budget Act of 2018, or the BBA, among other things, amends the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the “donut hole.” In July 2018, CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 2018, a Texas U.S. District Court Judge ruled that the ACA is unconstitutional in its entirety because the “individual mandate” was repealed by Congress as part of the Tax Act. While the Texas U.S. District Court Judge, as well as the Trump administration and CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the ACA will impact the ACA and our business.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013, and due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2027, unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have an adverse effect on customers for our product candidates, if approved, and, accordingly, our financial operations.

Additionally, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the Trump administration’s budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Further, the Trump administration released a “Blueprint”, or plan, to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. The Department of Health and Human Services has already started the process of soliciting feedback on some of these measures and, at the same, is immediately implementing others under its existing authority. For example, in September 2018, CMS announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019, and in October 2018, CMS proposed a new rule that would require direct-to-consumer television advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product. Although a number of these and other proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

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

We expect that these and 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 receive for any approved drug. 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 drugs.

In addition, FDA regulations and guidance may be revised or reinterpreted by the FDA in ways that may significantly affect our business and our products. The Trump administration has also taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict how these requirements will be interpreted and implemented and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose restrictions on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted. Any new regulations or guidance, including implementation of or new guidance regarding the frameworks for compounding under Sections 503A and 503B of the FDCA, or revisions or reinterpretations of existing regulations or guidance, may impose additional costs or lengthen FDA review times for PB2452, PB1046 or any future product candidates. We cannot determine how changes in regulations, statutes, policies, or interpretations when and if issued, enacted or adopted, may affect our business in the future. Such changes could, among other things, require:

- additional clinical trials to be conducted prior to obtaining approval;
- changes to manufacturing methods;
- recalls, replacements, or discontinuance of one or more of our products; and
- additional recordkeeping.

Such changes would likely require substantial time and impose significant costs, or could reduce the potential commercial value of PB2452, PB1046 or other product candidates, and could materially harm our business and our financial results. In addition, delays in receipt of or failure to receive regulatory clearances or approvals for any other products would harm our business, financial condition, and results of operations.

Our business activities may be subject to the Foreign Corrupt Practices Act, or FCPA, and similar anti-bribery and anti-corruption laws.

Our business activities may be subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers are subject to regulation under the FCPA. Recently the SEC and Department of Justice have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies. There is no certainty that all of our employees, agents, suppliers, manufacturers, contractors, or collaborators, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers, or our employees, the closing down of facilities, including those of our suppliers and manufacturers,

requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries as well as difficulties in manufacturing or continuing to develop our products, and could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees, and our business, prospects, operating results, and financial condition.

Risks Related to Employee Matters and Managing Our Growth

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

We are highly dependent on the management, development, clinical, financial and business development expertise of our executive officers, particularly Jonathan P. Mow, our Chief Executive Officer. Each of our executive officers may currently terminate their employment with us at any time. We do not maintain “key person” insurance for any of our executives or employees.

Recruiting and retaining qualified scientific and clinical personnel and, if we progress the development of our product pipeline toward scaling up for commercialization, manufacturing and sales and marketing personnel, will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and 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 successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel 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. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

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

As of December 31, 2018, we had 22 full-time employees. As our development progresses, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of clinical product development, regulatory affairs and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

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

We are exposed to the risk that our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, suppliers and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates FDA regulations, including those laws requiring the reporting of true, complete and accurate information to the FDA, manufacturing standards, federal and state healthcare laws and regulations, and laws that require the true, complete and accurate reporting of financial information or data. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct by these parties could also involve the improper use of individually identifiable information, including, without limitation, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, including, without limitation, damages, fines, disgorgement, individual imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations.

Risks Related to Ownership of Our Common Stock and Our Status as a Public Company

An active trading market for our common stock may not continue to be developed or sustained.

Prior to our initial public offering, there was no public market for our common stock, and we cannot assure you that an active trading market for our shares will continue to develop or be sustained. As a result, it may be difficult for you to sell shares at an attractive price or at all.

The trading price of the shares of our common stock may be volatile, and purchasers of our common stock could incur substantial losses.

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

- the commencement, enrollment or results of our clinical trials of PB2452, PB1046 and any future clinical trials we may conduct, or changes in the development status of our product candidates;
- any delay in our regulatory filings for PB2452, PB1046 or any other product candidate we may develop, and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings, including without limitation the FDA's issuance of a "refusal to file" letter or a request for additional information;
- adverse results from, delays in or termination of clinical trials;
- adverse regulatory decisions, including failure to receive regulatory approval of our product candidates;
- unanticipated serious safety concerns related to the use of PB2452, PB1046 or any other product candidate;
- changes in financial estimates by us or by any equity research analysts who might cover our stock;

- conditions or trends in our industry;
- changes in the market valuations of similar companies;
- stock market price and volume fluctuations of comparable companies and, in particular, those that operate in the biopharmaceutical industry;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- announcements by us or our competitors of significant acquisitions, strategic partnerships or divestitures;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- investors' general perception of our company and our business;
- recruitment or departure of key personnel;
- overall performance of the equity markets;
- trading volume of our common stock;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation;
- changes in the structure of healthcare payment systems;
- general political and economic conditions; and
- other events or factors, many of which are beyond our control.

In addition, in the past, stockholders have initiated class action lawsuits against pharmaceutical and biotechnology companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources from our business.

If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our stock price and trading volume could decline.

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

A significant portion of our total outstanding shares are restricted from immediate resale but may be sold into the market in the near future. This could cause the market price of our common stock to drop significantly, even if our business is doing well.

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

As of March 15, 2019, we had 24,498,425 outstanding shares of common stock. Of these shares, approximately 9.9 million shares are freely tradable and substantially all of the remaining shares of common stock will be available for sale in the public market beginning in April 2019 following the scheduled expiration of lock-up agreements between some of our stockholders and the underwriters entered into in connection with our initial public offering. Citigroup Global Markets Inc. and Cowen and Company, LLC may release these stockholders from their lock-up agreements with the underwriters at any time and without notice, which would allow for earlier sales of shares in the public market.

In addition, we have filed registration statements on Form S-8 registering the issuance of common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. Shares registered under these registration statements on Form S-8 will be available for sale in the public market subject to vesting arrangements and exercise of options, the lock-up agreements described above and the restrictions of Rule 144 in the case of our affiliates.

Additionally, the holders of approximately 13.9 million shares of our common stock, or their transferees, will have rights, subject to some conditions, to require us to file one or more registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. If we were to register the resale of these shares, they could be freely sold in the public market. If these additional shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

The issuance of additional stock in connection with financings, acquisitions, investments, our equity incentive plan or otherwise will dilute all other stockholders.

Our certificate of incorporation authorizes us to issue up to 200,000,000 shares of common stock and up to 10,000,000 shares of preferred stock with such rights and preferences as may be determined by our board of directors. Subject to compliance with applicable rules and regulations, in the future we may issue common stock or other securities convertible into shares of our common stock from time to time in connection with a financing, acquisition, investment, our equity incentive plan or otherwise. The number of new shares of our common stock issued in connection with raising additional capital could constitute a material portion of the then outstanding shares of our common stock, which could result in substantial dilution to our existing stockholders and cause the market price of our common stock to decline.

Provisions in our corporate charter documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management and hinder efforts to acquire a controlling interest in us, and the market price of our common stock may be lower as a result.

There are provisions in our certificate of incorporation and bylaws that may make it difficult for a third party to acquire, or attempt to acquire, control of our company, even if a change of control was considered favorable by you and other stockholders. For example, our board of directors has the authority to issue up to 10,000,000 shares of preferred stock. The board of directors can fix the price, rights, preferences, privileges, and restrictions of the preferred stock without any further vote or action by our stockholders. The issuance of shares of preferred stock may delay or prevent a change of control transaction. As a result, the market price of our common stock and the voting and other rights of our stockholders may be adversely affected. An issuance of shares of preferred stock may result in the loss of voting control to other stockholders.

Our charter documents also contain other provisions that could have an anti-takeover effect, including:

- only one of our three classes of directors will be elected each year;
- stockholders will not be entitled to remove directors other than by a 66 2/3% vote and only for cause;
- stockholders will not be permitted to take actions by written consent;
- stockholders cannot call a special meeting of stockholders; and
- stockholders must give advance notice to nominate directors or submit proposals for consideration at stockholder meetings.

In addition, we are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law, which regulates corporate acquisitions by prohibiting Delaware corporations from engaging in specified business combinations with particular stockholders of those companies. These provisions could discourage potential acquisition proposals and could delay or prevent a change of control transaction. They could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

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

Our executive officers, directors and current beneficial owners of 5% or more of our common stock and their respective affiliates beneficially own a significant percentage of our outstanding common stock. As a result, these persons, acting together, would be able to significantly influence all matters requiring stockholder approval, including the election and removal of directors, any merger, consolidation, sale of all or substantially all of our assets, or other significant corporate transactions.

Some of these persons or entities may have interests different than yours. For example, because many of these stockholders purchased their shares at prices substantially below the current market price of our common stock and have held their shares for a longer period, they may be more interested in selling our company to an acquirer than other investors, or they may want us to pursue strategies that deviate from the interests of other stockholders.

We are an “emerging growth company” and a “smaller reporting company” and, as a result of the reduced disclosure and governance requirements applicable to emerging growth companies and smaller reporting companies, our common stock may be less attractive to investors.

We are an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and we intend to take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- not being required to comply with the auditor attestation requirements 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 in our periodic reports, proxy statements and registration statements; and
- not being required to hold a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the closing of our initial public offering, (b) in which we have total annual gross revenue of at least \$1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the prior June 30th, and (2) the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior three-year period.

Under Section 107(b) of the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards until such time as those standards 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. Even after we no longer qualify as an emerging growth company, we may, under certain circumstances, still qualify as a “smaller reporting company,” which would allow us to take advantage of many of the same exemptions from disclosure requirements, including reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements.

If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.

We are subject to the reporting requirements of the Securities Exchange Act of 1934, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and the rules and regulations of the stock market on which our common stock is listed. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting.

Commencing with our fiscal year ending December 31, 2019, we must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal control over financial reporting in our Form 10-K filing for that year, as required by Section 404 of the Sarbanes-Oxley Act. This will require that we incur substantial additional professional fees and internal costs to expand our accounting and finance functions and that we expend significant management efforts. To date, we have never been required to test our internal control within a specified period, and, as a result, we may experience difficulty in meeting these reporting requirements in a timely manner.

We may identify weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system’s objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our stock could decline and we could be subject to sanctions or investigations by the stock exchange on which our common stock is listed, the Securities and Exchange Commission, or the SEC, or other regulatory authorities.

We will have broad discretion in the use of our cash and cash equivalents, including the net proceeds from our initial public offering.

We will have broad discretion over the use of our cash and cash equivalents, including the net proceeds from our recent initial public offering. You may not agree with our decisions, and our use of these cash and cash equivalents may not yield any return on your investment. We expect to use our existing cash and cash equivalents to advance PB2452, advance PB1046, fund development of our ELP technology and preclinical programs and for working capital and general corporate purposes. In addition, we may use a portion of our cash and cash equivalents to pursue our strategy to in-license or acquire additional product candidates. Our failure to apply our cash and cash equivalents effectively could compromise our ability to pursue our growth strategy and we might not be able to yield a significant return, if any, on our investment of these cash and cash equivalents. You will not have the opportunity to influence our decisions on how to use these cash and cash equivalents.

New or future changes to tax laws could materially adversely affect our company.

On December 22, 2017, President Trump signed into law H.R. 1, “An Act to provide for reconciliation pursuant to titles II and V of the concurrent resolution on the budget for fiscal year 2018”, informally titled the Tax Cuts and Jobs Act, or, the Tax Act, which significantly revises the U.S. Internal Revenue Code of 1986, as amended. The Tax Act, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted taxable income (except for certain small businesses), effective for net operating losses incurred in taxable years beginning after December 31, 2017, limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits, including the orphan drug credit. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the Tax Act is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain how various states will respond to the Tax Act. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. We urge you to consult with your legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

Our effective tax rate may fluctuate, and we may incur obligations in tax jurisdictions in excess of accrued amounts.

We are subject to taxation in more than one tax jurisdiction. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each of such places. Nevertheless, our effective tax rate may be different than experienced in the past due to numerous factors, including passage of the newly enacted federal income tax law, changes in the mix of our profitability from jurisdiction to jurisdiction, the results of examinations and audits of our tax filings, our inability to secure or sustain acceptable agreements with tax authorities, changes in accounting for income taxes and changes in tax laws. Any of these factors could cause us to experience an effective tax rate significantly different from previous periods or our current expectations and may result in tax obligations in excess of amounts accrued in our financial statements.

We might not be able to utilize a significant portion of our net operating loss carryforwards.

At December 31, 2018, we had federal and Pennsylvania net operating loss, or NOL, carryforwards of \$111.9 million, and \$105.9 million, respectively. The federal NOLs generated prior to 2018 may be used to offset up to 100% of future taxable income and will begin to expire in 2022, unless previously utilized. These net operating loss carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the Tax Act, federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited. It is uncertain how various states will respond to the Tax Act. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an “ownership change,” which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation’s ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. We may experience ownership changes as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. If an ownership change occurs and our ability to use our net operating loss carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations.

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 gains and you may never receive a return on your investment.

You should not rely on an investment in our common stock to provide dividend income. We have not declared or paid cash dividends on our common stock to date. We currently intend to retain our future earnings, if any, to fund the development and growth of our business. In addition, the terms of any existing or future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future. Investors seeking cash dividends should not purchase our common stock.

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

As a public company listed in the United States, we are incurring significant additional legal, accounting and other costs, which we anticipate could be between \$1.0 million and \$2.0 million annually. These additional costs could negatively affect our financial results. In addition, changing laws, regulations and standards relating to corporate governance and public disclosure, including regulations implemented by the SEC and the Nasdaq Stock Market, may increase legal and financial compliance costs and make some activities more time-consuming. These laws, regulations and standards are subject to varying interpretations and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expense and a diversion of management's time and attention from revenue-generating activities to compliance activities. If notwithstanding our efforts to comply with new laws, regulations and standards, we fail to comply, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

Failure to comply with these rules might also make it more difficult for us to obtain some types of insurance, including director and officer liability insurance, and we might be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, on committees of our board of directors or as members of senior management.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware and the federal district courts of the United States of America will be the exclusive forums for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim for breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (3) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws or (4) any action asserting a claim governed by the internal affairs doctrine. Our amended and restated certificate of incorporation further provides that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act.

These exclusive forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. For example, stockholders who do bring a claim in the Court of Chancery could face additional litigation costs in pursuing any such claim, particularly if they do not reside in or near the State of Delaware. The Court of Chancery and federal district courts may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments or results may be more favorable to us than to our stockholders. Some companies that adopted a similar federal district court forum selection provision are currently subject to a suit in the Chancery Court of Delaware by stockholders who assert that the provision is not enforceable. If a court were to find either choice of forum provision contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

Recently, the Court of Chancery of the State of Delaware issued an opinion invalidating the federal district court exclusive forum provision. In light of that recent decision, we will not attempt to enforce this provision of our amended and restated certificate of incorporation, unless the decision is reversed on appeal. As a result, we may incur additional costs associated with resolving disputes that would otherwise be restricted by that provision in other jurisdictions, which could seriously harm our business. However, if the decision is reviewed on appeal and ultimately overturned by the Delaware Supreme Court, we would enforce the federal district court exclusive forum provision.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

We lease 16,000 square feet of research and development and administrative space in Malvern, Pennsylvania pursuant to a lease agreement that expires in September 2023. We also lease 4,000 square feet of administrative space in San Diego, California pursuant to a lease agreement that expires in October 2022. We believe that our existing facilities are suitable and adequate to meet our current needs. We intend to add new facilities or expand existing facilities as we add employees, and we believe that suitable additional or substitute space will be available as needed to accommodate any such expansion of our operations.

Item 3. Legal Proceedings.

We are not subject to any material legal proceedings. From time to time, we may be involved in various claims and legal proceedings relating to claims arising out of our operations. We are not currently a party to any legal proceedings that, in the opinion of our management, are likely to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Item 4. Mine Safety Disclosures.

Not applicable.

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

Market Information for Common Stock

Our common stock is listed on The Nasdaq Global Market under the symbol "PHAS."

Holders of Record

As of March 15, 2019, we had 93 holders of record of our common stock, which excludes stockholders whose shares were held in nominee or street name by brokers. The actual number of common stockholders is greater than the number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend Policy

We have never paid cash dividends on any of our capital stock and currently intend to retain our future earnings, if any, to fund the development and growth of our business.

Use of Proceeds from Initial Public Offering

On October 17, 2018, our registration statement on Form S-1, as amended (File No. 333-227474) was declared effective by the SEC in connection with our initial public offering pursuant to which we sold 9,200,000 shares of common stock, \$0.001 par value per share at a public offering price of \$5.00 per share. Citigroup Global Markets, Inc., Cowen and Company, LLC and Stifel, Nicolaus & Company, Incorporated acted as joint book-running managers and Needham & Company, LLC acted as co-manager for the offering. The net proceeds from this sale, after underwriting discounts and offering expenses, were \$39.9 million.

On November 5, 2018, the offering closed with respect to an additional 664,666 shares purchased by the underwriters pursuant to the underwriters' option to purchase additional shares. The net proceeds from this sale, after underwriting discounts, were approximately \$3.1 million.

In connection with our initial public offering, no payments were made by us to directors, officers or persons owning ten percent or more of our common stock or to their associates or to our affiliates. There has been no material change in the planned use of proceeds from our initial public offering from that described in the final prospectus related to the offering, dated October 17, 2018, as filed with the SEC on October 19, 2018.

Unregistered Sales of Equity Securities

The following sets forth information as to all securities we sold in 2018 which were not registered under the Securities Act:

Series D Redeemable Preferred Stock

In August 2018, we issued and sold an aggregate of 1,842,959 shares of Series D redeemable preferred stock at a price per share equal to \$9.659 for net proceeds of \$17.7 million and issued warrants to purchase 368,582 shares of Series C-1 redeemable preferred stock at an exercise price of \$0.12 per share. Concurrent with this financing, all of our previously outstanding convertible promissory notes, including accrued interest thereon, were converted into 2,080,209 shares of Series D redeemable preferred stock.

Common Stock Issued upon Conversion of Preferred Stock

In October 2018, upon the closing of our initial public offering, all shares of our then-outstanding convertible preferred stock were automatically converted into 13,200,115 shares of common stock. The issuance of such shares of common stock was exempt from registration under Section 3(a)(9) of the Securities Act.

Common Stock Issued upon Exercises of Warrants

In October 2018, in connection with the closing of our initial public offering, we issued 58,248 shares of common stock upon the exercise of warrants for cash at a weighted-average exercise price of \$0.12 per share.

We also issued 560,838 shares of common stock upon the net exercise of warrants at a weighted-average exercise price of \$0.12 per share. In conjunction with this transaction, an aggregate of 13,800 shares of common stock otherwise issuable pursuant to such warrants were forfeited as consideration for the exercise. The issuance of these securities was exempt from registration under Section 3(a)(9) of the Securities Act.

Options

Prior to the filing of our Registration Statement on Form S-8 (File No. 333-227935) in October 2018, we granted under our Amended and Restated 2002 Stock Plan options to purchase an aggregate of 260,302 shares of common stock to a total of 25 employees, consultants and directors, having exercise prices ranging from \$2.26 to \$4.65 per share.

Except as otherwise noted, we claimed exemption from registration under the Securities Act for the sales and issuances of securities in the transactions described above under Section 4(a)(2) of the Securities Act in that such sales and issuances did not involve a public offering or under Rule 701 promulgated under the Securities Act, or Rule 701, in that they were offered and sold either pursuant to written compensatory plans or pursuant to a written contract relating to compensation, as provided by Rule 701.

All of the foregoing securities are deemed restricted securities for purposes of the Securities Act. All certificates representing the issued securities described in this Item 5 included appropriate legends setting forth that the securities had not been registered and the applicable restrictions on transfer.

The information presented in this Item 5 gives effect to a 11.0634-for-1 reverse stock split, which became effective on October 4, 2018.

Purchases of Equity Securities by the Issuer and Affiliated Parties

None.

Item 6. Selected Financial Data.

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act and are not required to provide the information required under this item.

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our financial statements and related notes and the related Management’s Discussion and Analysis of Financial Condition and Results of Operations included in this Annual Report on Form 10-K.

Overview

We are a clinical-stage biopharmaceutical company focused on the development and commercialization of novel therapies to treat orphan diseases, with an initial focus on cardiopulmonary indications. Our lead product candidate, PB2452, is a novel reversal agent for the antiplatelet drug ticagrelor, which we are developing for the treatment of patients experiencing major bleeding or those who require urgent surgery. We recently completed a Phase 1 clinical trial of PB2452 in healthy subjects and intend to initiate a Phase 2b clinical trial in healthy older subjects in the first half of 2019. Our second product candidate, PB1046, is a once-weekly fusion protein currently in a Phase 2b clinical trial for the treatment of pulmonary arterial hypertension, or PAH. PB1046 utilizes our proprietary half-life extending elastin-like polypeptide, or ELP, technology, which also serves as the engine for our preclinical pipeline.

We have a limited operating history. Since our inception in 2002, our operations have focused on developing our clinical and preclinical product candidates and our proprietary ELP technology, organizing and staffing our company, business planning, raising capital, establishing our intellectual property portfolio and conducting clinical trials and preclinical studies. We do not have any product candidates approved for sale and have not generated any revenue from product sales. Since inception, we have funded our operations through the sale of equity and debt securities and our term loans with Silicon Valley Bank, or SVB, and WestRiver Innovation Lending Fund VIII, L.P., or WestRiver.

In 2018, we received \$60.7 million in aggregate net proceeds from our initial public offering and the sale of our Series D convertible preferred stock and \$4.0 million in net proceeds from borrowings under our term loan with SVB. As of December 31, 2018, we had cash and cash equivalents of \$61.0 million. We believe that our existing cash and cash equivalents are sufficient to fund our operating expenses and capital requirements into the second quarter of 2020. See “—Liquidity and Capital Resources.”

Since our inception, we have incurred significant operating losses. Our net loss was \$23.8 million for the year ended December 31, 2018. As of December 31, 2018, we had an accumulated deficit of \$122.9 million. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate that our expenses will increase significantly in connection with our ongoing activities, as we:

- continue our ongoing clinical trials of PB2452 and PB1046, as well as initiate and complete additional clinical trials, as needed;
- pursue regulatory approvals for PB2452 as a reversal agent for the antiplatelet drug ticagrelor and PB1046 for the treatment of PAH;
- seek to discover and develop additional clinical and preclinical product candidates;
- scale up our clinical and regulatory capabilities;
- establish a commercialization infrastructure and scale up external manufacturing and distribution capabilities to commercialize any product candidates for which we may obtain regulatory approval, including PB2452 and PB1046;
- adapt our regulatory compliance efforts to incorporate requirements applicable to marketed products, if any;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, manufacturing and scientific personnel;

- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and
- incur additional legal, accounting and other expenses in operating as a public company.

FINANCIAL OVERVIEW

Components of Operating Results

Grant Revenues

Grant revenues are derived from government grants that support our efforts on specific research projects. We recognize grant revenue when there is reasonable assurance of compliance with the conditions of the grant and reasonable assurance that the grant revenue will be received.

Research and Development Expense

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

- expenses incurred under agreements with contract research organizations, or CROs, as well as investigative sites and consultants that conduct our clinical trials and preclinical studies;
- manufacturing and supply scale-up expenses and the cost of acquiring and manufacturing preclinical and clinical trial supply and potential commercial supply, including manufacturing validation batches;
- outsourced professional scientific development services;
- employee-related expenses, which include salaries, benefits and stock-based compensation;
- expenses relating to regulatory activities; and
- laboratory materials and supplies used to support our research activities.

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 our research and development expense to increase significantly over the next several years as we increase personnel costs, including stock-based compensation, conduct our later-stage clinical trials for PB2452 and PB1046 and conduct other preclinical studies and clinical trials and prepare regulatory filings for our product candidates.

The successful development of our product candidates is highly uncertain. At this time, we cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the remainder of the development of, or when, if ever, material net cash inflows may commence from our product candidates. This uncertainty is due to the numerous risks and uncertainties associated with the duration and cost of clinical trials, which vary significantly over the life of a project as a result of many factors, including:

- delays in regulators or institutional review boards authorizing us or our investigators to commence our clinical trials or in our ability to negotiate agreements with clinical trial sites or contract research organizations;
- our ability to secure adequate supply of product candidates for our trials;
- the number of clinical sites included in the trials;
- the length of time required to enroll suitable patients;
- the number of patients that ultimately participate in the trials;
- the number of doses patients receive;

- any side effects associated with our product candidates;
- the duration of patient follow-up; and
- the results of our clinical trials.

Our expenditures are subject to additional uncertainties, including the terms and timing of regulatory approvals, and the expense of filing, prosecuting, defending and enforcing any patent claims or other intellectual property rights. We may never succeed in achieving regulatory approval for our product candidates. We may obtain unexpected results from our clinical trials. We may elect to discontinue, delay or modify clinical trials of our product candidates. A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the Food and Drug Administration, or the FDA, or other regulatory authorities were to require us to conduct clinical trials beyond those that we currently anticipate, or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development. Product commercialization will take several years and millions of dollars in development costs.

General and Administrative Expense

General and administrative expense consists principally of salaries and related costs for personnel in executive and administrative functions, including stock-based compensation, travel expenses and recruiting expenses. Other general and administrative expense includes professional fees for legal, accounting and tax-related services and insurance costs.

We anticipate that our general and administrative expense will increase as a result of increased payroll, expanded infrastructure and higher consulting, legal and tax-related services associated with maintaining compliance with stock exchange listing and SEC requirements, accounting and investor relations costs, and director and officer insurance premiums associated with being a public company. We anticipate the additional costs for these services will increase our general and administrative expense.

Interest Expense

Interest expense consists of interest expense on our convertible promissory notes and term loan.

Change in Fair Value of Warrant and Derivative Liabilities

Change in fair value of warrant and derivative liabilities reflects the revaluation at each reporting date of our redeemable convertible preferred stock warrants and the conversion option on our convertible promissory notes, respectively. Subsequent to the conversion of all outstanding shares of our preferred stock into common stock in connection with the closing of our initial public offering in October 2018, we are no longer required to remeasure the warrant liability for periods following the closing of the initial public offering. Additionally, in August 2018 all of our previously outstanding convertible promissory notes converted with the sale and issuance of the Series D redeemable preferred stock. As such, we will no longer be required to remeasure the conversion option for the periods following the closing of that financing.

License Agreements

MedImmune Limited

In November 2017, we entered into an exclusive license agreement, or the MedImmune License, with MedImmune Limited, or MedImmune, a wholly owned subsidiary of AstraZeneca plc. Pursuant to the MedImmune License, MedImmune granted us an exclusive, worldwide license under certain patent rights owned or controlled by MedImmune to develop and commercialize any products covered by the MedImmune License, or the MedImmune licensed products, for the treatment, palliation, diagnosis or prevention of any human disorder or condition. Under the MedImmune License, we paid MedImmune an upfront fee of \$0.1 million. We are also required to pay MedImmune: quarterly fees relating to technical services provided by MedImmune; up to \$18.0 million in clinical

and regulatory milestone fees; up to \$50.0 million in commercial milestone fees; and mid-single digit to low-teen royalty percentages on net sales of MedImmune licensed products, subject to reduction in specified circumstances. In addition, the MedImmune License offers an option for third-party product storage costs. As of December 31, 2018, we have paid \$0.5 million under the MedImmune License.

Duke University

In October 2006, we entered into an exclusive license agreement, or the Duke License, with Duke University, or Duke, which we most recently amended in May 2017. Pursuant to the Duke License, Duke granted us an exclusive, worldwide license under certain patent rights owned or controlled by Duke, and a non-exclusive, worldwide license under certain know-how of Duke, to develop and commercialize any products covered by the Duke License, or Duke licensed products, relating to ELPs. Under the Duke License, we paid Duke an upfront fee of \$37,000, additional fees in connection with amendments to the Duke License of \$0.2 million and other additional licensing fees of \$0.2 million. In consideration for license rights granted to us, we initially issued Duke 24,493 shares of our common stock. Until we reached a certain stipulated equity milestone, which we reached in October 2007, we were obligated to issue additional shares of common stock to Duke from time to time so that its aggregate ownership represented 7.5% of our issued and outstanding capital stock. We are also required to pay Duke: up to \$2.2 million in regulatory and clinical milestone fees; up to \$0.4 million in commercial milestone fees; low single-digit royalty percentages on net sales of Duke licensed products, with minimum aggregate royalty payments of \$0.2 million payable following our achievement of certain commercial milestones; and up to the greater of \$0.3 million or a low double-digit percentage of the fees we receive from a third party in consideration of forming a strategic alliance with respect to certain patent rights covered under the Duke License. We also must pay Duke the first \$1.0 million of non-royalty payments we receive from a sublicensee, and thereafter a low double-digit percentage of any additional nonroyalty payments we receive. As of December 31, 2018, we have not paid any amounts under the Duke License. We are also required to apply for, prosecute and maintain all U.S. and foreign patent rights under the Duke License.

Results of Operations

Comparison of the Years Ended December 31, 2018 and 2017

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

	Year Ended December 31,		Change
	2018	2017	
Grant revenues	\$ 668	\$ —	\$ 668
Operating expenses			
Research and development	15,455	6,210	9,245
General and administrative	4,857	2,328	2,529
Total operating expenses	20,312	8,538	11,774
Loss from operations	(19,644)	(8,538)	(11,106)
Other income (expense)			
Interest income	387	52	335
Interest expense	(3,924)	(2,723)	(1,201)
Change in fair value of warrant liability	11	1,019	(1,008)
Change in fair value of derivative liability	(676)	(57)	(619)
Total other income (expense)	(4,202)	(1,709)	(2,493)
Net loss	\$ (23,846)	\$ (10,247)	\$ (13,599)

Grant Revenues

Grant revenues were \$0.7 million for the year ended December 31, 2018, as we incurred allowable costs qualifying for reimbursement under our government grants. We did not receive any grant revenues for the year ended December 31, 2017.

Research and Development Expense

Research and development expense was \$15.5 million for the year ended December 31, 2018, compared to \$6.2 million for the year ended December 31, 2017. The increase of \$9.2 million was primarily attributable to increased costs associated with preclinical and clinical development activities largely related to PB2452 and PB1046.

The following table summarizes our research and development expense by functional area for the years ended December 31, 2018 and 2017 (in thousands):

	Year Ended December 31,		Change
	2018	2017	
Preclinical and clinical development	\$ 11,857	\$ 2,944	\$ 8,913
Compensation and related benefits	2,789	2,473	316
Stock-based compensation	124	37	87
Facilities expense	463	389	74
Other	222	367	(145)
Total research and development expense	<u>\$ 15,455</u>	<u>\$ 6,210</u>	<u>\$ 9,245</u>

The following table summarizes our research and development expense by product candidate for the years ended December 31, 2018 and 2017 (in thousands):

	Year Ended December 31,		Change
	2018	2017	
External research and development expense by program			
PB2452	\$ 6,726	\$ 579	\$ 6,147
PB1046	4,542	1,918	2,624
Unallocated research and development expense			
Compensation and stock-based compensation	2,913	2,510	403
Other research and development	1,274	1,203	71
Total research and development expense	<u>\$ 15,455</u>	<u>\$ 6,210</u>	<u>\$ 9,245</u>

General and Administrative Expense

General and administrative expense was \$4.9 million for the year ended December 31, 2018, compared to \$2.3 million for the year ended December 31, 2017. The increase of \$2.5 million was primarily attributable to an increase in professional services including legal, marketing and other consulting services of \$1.4 million, an increase in employee compensation expense of \$0.7 million, an increase in insurance expenses of \$0.3 million and an increase in business travel-related expenses of \$0.2 million.

Interest Expense

Interest expense was \$3.9 million for the year ended December 31, 2018, compared to \$2.7 million for the year ended December 31, 2017. The increase of \$1.2 million was partially attributable to an additional \$8.1 million in borrowings pursuant to our convertible promissory notes entered into in October 2017. Additionally, we entered into our term loan in October 2017, pursuant to which we borrowed \$3.5 million in November 2017, \$2.0 million in April 2018 and \$2.0 million in August 2018, which also contributed to the increase in interest expense year over year.

Change in Fair Value of Warrant Liability

Change in fair value of warrant liability resulted in other income of \$11,000 for the year ended December 31, 2018, compared to other income of \$1.0 million for the year ended December 31, 2017. The preferred stock warrants were subject to remeasurement at each reporting period, with changes in fair value recorded in the statement of operations. The outstanding preferred stock warrants converted into common stock warrants upon the completion of our initial public offering.

Change in Fair Value of Derivative Liability

Change in fair value of derivative liability was \$0.7 million of expense for the year ended December 31, 2018, compared to \$0.1 million of expense for the year ended December 31, 2017. The conversion option related to our convertible promissory notes was subject to remeasurement at each reporting period, with changes in fair value recorded in the statement of operations. The convertible promissory notes converted into redeemable convertible preferred stock in August 2018 upon the sale of the Series D redeemable convertible preferred stock.

Liquidity and Capital Resources

Since our inception, we have not generated any revenue from product sales and have incurred net losses and negative cash flows from our operations. We have financed our operations since our inception primarily through the sales of equity and debt securities and borrowings under our term loans with SVB and WestRiver. As of December 31, 2018, we had cash and cash equivalents of \$61.0 million.

October 2017 Loan Agreement with SVB

In October 2017, we entered into a loan and security agreement, or the SVB Loan, with SVB, which provided that we could borrow up to \$7.5 million, issuable in three separate tranches, or Growth Capital Advances, of \$3.5 million, \$2.0 million and \$2.0 million, each available upon achievement of certain clinical and regulatory milestones. We drew each of the tranches in November 2017, April 2018 and August 2018, respectively. The maturity date of the SVB Loan was June 1, 2020, which was extended to December 31, 2020 when we drew on the third tranche. The SVB Loan was interest-only through July 31, 2018, which was extended to December 31, 2018 when we drew on the third tranche.

In addition to interest and principal payments, we were required to make a final payment equal to 7% of the original aggregate principal amount of the Growth Capital Advances. We had the option to prepay all, but not less than all, of the borrowed amounts, provided that we would be obligated to pay a prepayment fee equal to (a) 3.0% of the outstanding principal balance of the applicable Growth Capital Advances if prepayment was made prior to the first anniversary of the effective date of the SVB Loan, (b) 2.0% of the outstanding principal balance of the applicable Growth Capital Advances if prepayment was made by the second anniversary of the effective date of the SVB Loan or (c) 1.0% of the outstanding principal balance of the applicable Growth Capital Advances if prepayment was made after the second anniversary of the effective date of the SVB Loan.

On March 25, 2019, we repaid the outstanding principal balance and accrued portion of the final payment under the SVB Loan in full using Tranche A from the 2019 Loan described below.

March 2019 Loan Agreement with SVB and WestRiver

On March 25, 2019, we entered into a term loan agreement, or the 2019 Loan, with SVB and WestRiver, pursuant to which we may borrow up to \$15.0 million, issuable in three separate tranches, or Advances, of \$7.5 million, or Tranche A, which was issued upon execution of the 2019 Loan, \$2.5 million, or Tranche B, available to be issued until May 31, 2019 and \$5.0 million, or Tranche C, which we will draw upon the achievement of certain regulatory milestones, or the Tranche C milestones.

The maturity date of the 2019 Loan is March 1, 2023. Under the terms of the 2019 Loan, we are to make interest-only payments through December 31, 2019 on Tranche A and Tranche B at a rate equal to the greater of the Prime Rate plus 1.00%, as defined in the 2019 Loan, or 6.5%, followed by an amortization period of 39 months of equal monthly payments of principal plus interest amounts until paid in full. The interest-only period will automatically be extended to June 30, 2020 if we achieve the Tranche C milestones, followed by an amortization period of 33 months of equal monthly payments of principal plus interest amounts until paid in full. In addition to and not in substitution for our regular monthly payments of principal plus accrued interest, we are required to make a final payment equal to 6% of the aggregate principal amount of the Advances on the maturity date.

We have agreed to issue to SVB and WestRiver warrants to purchase an aggregate of 37,606 shares of our common stock when we draw on Tranche A, an aggregate of 12,131 shares of our common stock on when we draw on Tranche B and an aggregate of 24,462 shares of our common stock when we draw on Tranche C, each with an exercise price of the lower of the average closing price of our common stock for the previous ten days of trading or the closing price on the day prior to funding. The warrants are immediately exercisable upon issuance and expire ten years from the date of issuance.

Upon execution of the 2019 Loan, we drew \$7.5 million from Tranche A and repaid the outstanding principal balance and accrued portion of the final payment for the SVB Loan in full. We also issued warrants to purchase 18,803 shares of our common stock to each of SVB and WestRiver, with exercise prices of \$4.73 per share.

Our obligations under the 2019 Loan are secured by a first priority security interest in substantially all of our current and future assets, excluding intellectual property. We are also obligated to comply with various other customary covenants, including restrictions on our ability to encumber our intellectual property assets.

Convertible Promissory Notes

In January 2017 and October 2017, we issued \$14.7 million of convertible promissory notes, or the 2017 Notes, to holders of Series C-1 redeemable convertible preferred stock. The 2017 Notes bore interest at the rate of 8%. The 2017 Notes had a stated maturity date of March 31, 2018. In October 2017, the noteholders entered into a subordination agreement with SVB, pursuant to which the noteholders agreed that they would not demand or receive any payment on the 2017 Notes until all amounts owed under the SVB Loan were repaid in full on June 1, 2020. In August 2018, all of the 2017 Notes were converted concurrent with the sale of our Series D redeemable convertible preferred stock.

As of December 31, 2018, we had cash and cash equivalents of \$61.0 million.

The following table summarizes our cash flows for each of the periods set forth below (in thousands):

	Year Ended December 31,	
	2018	2017
Net cash used in operating activities	\$ (17,053)	\$ (8,259)
Net cash used in investing activities	(119)	(216)
Net cash provided by financing activities	64,797	18,166
Net increase in cash and cash equivalents	\$ 47,625	\$ 9,691

Operating Activities

Net cash used in operating activities was \$17.1 million during the year ended December 31, 2018. The use of cash primarily related to our net loss of \$23.8 million, adjusted for non-cash charges primarily related to \$3.7 million for non-cash interest expense, \$0.7 million for the change in the fair value of the derivative liability and a \$2.0 million change in our operating assets and liabilities. The change in our operating assets and liabilities was principally due to a \$3.3 million increase in accounts payable and accrued expenses, partially offset by a \$1.0 million increase in prepaid expenses, all as a result of increased clinical activities for our ongoing clinical trials of PB2452 and PB1046.

Net cash used in operating activities was \$8.3 million during the year ended December 31, 2017. The use of cash primarily related to our net loss of \$10.2 million, adjusted for non-cash charges principally related to \$2.7 million for non-cash interest expense and \$1.0 million for the change in the fair value of the warrant liability.

Investing Activities

Net cash used in investing activities was \$0.1 million for the purchase of property and equipment during the year ended December 31, 2018. Net cash used in investing activities was \$0.2 million for the purchase of property and equipment during the year ended December 31, 2017.

Financing Activities

Net cash provided by financing activities was \$64.8 million during the year ended December 31, 2018, consisting primarily of \$43.0 million in net proceeds from our initial public offering, \$17.7 million from the issuance of the Series D redeemable convertible preferred stock and \$4.0 million from the issuance of our term loan with SVB. Net cash provided by financing activities was \$18.2 million during the year ended December 31, 2017 consisting of net proceeds from the issuance of convertible promissory notes and our term loan with SVB.

Funding Requirements

To date, we have not generated any revenues from the commercial sale of approved drug products, and we do not expect to generate substantial revenue for at least the next several years. If we fail to complete the development of our product candidates in a timely manner or fail to obtain their regulatory approval, our ability to generate future revenue will be compromised. We do not know when, or if, we will generate any revenue from our product candidates, and we do not expect to generate significant revenue unless and until we obtain regulatory approval of, and commercialize, our product candidates. We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, continue or initiate clinical trials of and seek marketing approval for our product candidates. In addition, if we obtain approval for any of our product candidates, we expect to incur significant commercialization expenses related to sales, marketing, manufacturing and distribution. We anticipate that we will need substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

We believe that our existing cash and cash equivalents are sufficient to fund our operating expenses and capital requirements into the second quarter of 2020. We intend to devote our existing cash and cash equivalents to advance our clinical and preclinical development programs. We have based our estimates 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 and commercialization of product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures necessary to complete the development of product candidates.

Our future capital requirements will depend on many factors, including:

- the progress and results of our ongoing and planned future clinical trials of PB2452 and PB1046 and our preclinical programs;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for any future product candidates we may decide to pursue;
- the extent to which we develop, in-license or acquire other product candidates and technologies;
- the number and development requirements of other product candidates that we may pursue;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- our ability to establish collaborations to commercialize PB1046 in the United States;
- our ability to establish collaborations to commercialize PB2452, PB1046 or any of our other product candidates outside the United States; and
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims.

Identifying potential product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes many 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 product candidates that we do not expect to be commercially available in the near term, if at all.

Our future commercial revenue, if any, will be derived from sales of products that we do not expect to be commercially available for several years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the terms of these equity securities or this debt may restrict our ability to operate. Any future debt financing and equity financing, if available, may involve agreements that include, covenants limiting and restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, entering into profit-sharing or other arrangements or declaring dividends. If we raise additional funds through government or private grants, collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us.

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 SEC rules and regulations.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with U.S. generally accepted accounting policies, or GAAP. The preparation of these financial statements requires us to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities as of the dates of the balance sheets and the reported amounts of expenses during the reporting periods. In accordance with GAAP, we evaluate our estimates and judgments on an ongoing basis. We believe the following accounting policies are the most critical to the judgments and estimates used in the preparation of our financial statements. See Note 2 to the financial statements appearing elsewhere in this Annual Report for a discussion of our significant accounting policies.

Accrued Research and Development Expense

The majority of our operating expenses to date have been incurred in research and development activities. As part of the process of preparing our financial statements, we are required to estimate expenses resulting from obligations under contracts with vendors, consultants and research organizations, in connection with conducting clinical and preclinical activities. The financial terms of these contracts are subject to negotiations which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided under such contracts. We reflect preclinical study and clinical trial expenses in our financial statements by matching those expenses with the period in which services and efforts are expended. We account for these expenses according to the progress of the preclinical study or clinical trial as measured by the timing of various aspects of the preclinical study or clinical trial, or related activities. Our accrual estimates are determined through review of the underlying contracts along with preparation of financial models taking into account discussions with research and other key personnel as to the progress of preclinical studies or clinical trials, or other services being conducted. During the course of a preclinical study or clinical trial, we will adjust the rate of expense recognition if actual results differ from our original estimates.

Recent Accounting Pronouncements

See Note 2 to the financial statements appearing elsewhere in this Annual Report for information concerning recent accounting pronouncements.

JOBS Act Transition Period

In April 2012, the JOBS Act was enacted. Section 107 of the JOBS Act provides that an “emerging growth company” 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 emerging growth company 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.

We are in the process of evaluating the benefits of relying on other exemptions and reduced reporting requirements under the JOBS Act. Subject to certain conditions, as an emerging growth company, we may rely on certain of these exemptions, including without limitation, (i) not providing an auditor’s attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and (ii) not complying with any requirement that may be adopted by the Public Company Accounting Oversight Board. We will remain an emerging growth company until the earliest to occur of (1) the last day of the fiscal year (a) ending December 31, 2023, which is the end of the fiscal year following the fifth anniversary of the completion of our initial public offering, (b) in which we have total annual gross revenues of at least \$1.07 billion or (c) in which we are deemed to be a “large accelerated filer” under the rules of the SEC, which means the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the prior June 30th, and (2) the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior three-year period.

Effect of Inflation

Inflation did not have a significant impact on our net sales, revenues or income from continuing operations in 2018 or 2017.

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

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act and are not required to provide the information required under this item.

Item 8. Financial Statements and Supplementary Data.

The information required by this Item 8 is set forth in our financial statements included in Part IV, Item 15 of this Annual Report on Form 10-K.

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

None.

Item 9A. Controls and Procedures.

Disclosure Controls and Procedures

We maintain “disclosure controls and procedures,” as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, that are designed to ensure that information required to be disclosed by us in reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in SEC rules and forms, and that such information is accumulated and communicated to our management, including our principal executive and our principal financial officers, as appropriate, to allow timely decisions regarding required disclosure.

With respect to the year ended December 31, 2018, under the supervision and with the participation of our management, we conducted an evaluation of the effectiveness of the design and operations of our disclosure controls and procedures. Based upon this evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures were effective as of December 31, 2018 to provide reasonable assurance that the information required to be disclosed by us in this Annual Report was (a) reported within the time periods specified by SEC rules and regulations and (b) communicated to our management, including our Chief Executive Officer and Chief Financial Officer, to allow timely decisions regarding any required disclosure.

Management's Report on Internal Control Over Financial Reporting

This Annual Report does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm as allowed by the SEC during the transition period for newly public companies.

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) that occurred during the fiscal year ended December 31, 2018 which have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations on Effectiveness of Internal Controls

In designing and evaluating the disclosure controls and procedures, management does not expect that our internal control over financial reporting will prevent or detect all errors and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control systems are met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. The design of any disclosure controls and procedures also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions. Our management, including our Chief Executive Officer and Chief Financial Officer, believes that our disclosure controls and procedures and internal control over financial reporting are designed to provide reasonable assurance of achieving their objectives and are effective at the reasonable assurance level. However, our management does not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent all errors and all fraud.

Item 9B. Other Information.

On March 25, 2019, we entered into a term loan agreement, or the 2019 Loan, with Silicon Valley Bank, or SVB, and WestRiver Innovation Lending Fund VIII, L.P., or WestRiver, pursuant to which we may borrow up to \$15.0 million, issuable in three separate tranches, or Advances, of \$7.5 million, or Tranche A, which was issued upon execution of the SVB and WestRiver Loan Agreement, \$2.5 million available to be issued until May 31, 2019, or Tranche B, and \$5.0 million, or Tranche C, which we will draw upon the achievement of certain regulatory milestones, or the Tranche C milestones.

The maturity date of the 2019 Loan is March 1, 2023. Under the terms of the 2019 Loan, we are to make interest-only payments through December 31, 2019 on Tranche A and Tranche B at a rate equal to the greater of the Prime Rate plus 1.00%, as defined in the 2019 Loan, or 6.5%, followed by an amortization period of 39 months of equal monthly payments of principal plus interest amounts until paid in full. The interest-only period will automatically be extended to June 30, 2020 if we achieve the Tranche C milestones, followed by an amortization period of 33 months of equal monthly payments of principal plus interest amounts until paid in full. We are required to make a final payment equal to 6% of the aggregate principal amount of the Advances on the maturity date.

We have agreed to issue to SVB and WestRiver warrants to purchase an aggregate of 37,606 shares of our common stock when we draw on Tranche A, an aggregate of 12,131 shares of our common stock on when we draw on Tranche B and an aggregate of 24,462 shares of our common stock when we draw on Tranche C, with an exercise price of the lower of the average closing price of our common stock for the previous ten days of trading or the closing price on the day prior to funding. The warrants are immediately exercisable upon issuance and expire ten years from the date of issuance.

Upon execution of the 2019 Loan, we drew \$7.5 million from Tranche A and repaid the outstanding principal balance and accrued portion of the final payment for our existing term loan with SVB in full. We also issued warrants to purchase 18,803 shares of our common stock to each of SVB and WestRiver, with exercise prices of \$4.73 per share.

Our obligations under the 2019 Loan are secured by a first priority security interest in substantially all of our current and future assets, excluding intellectual property. We are also obligated to comply with various other customary covenants, including restrictions on our ability to encumber our intellectual property assets.

This summary of the 2019 Loan is qualified in its entirety by reference to the full text of the 2019 Loan, which is filed as Exhibit 10.13 to this Annual Report and incorporated by reference herein.

PART III

We will file a definitive Proxy Statement for our 2019 Annual Meeting of Stockholders, or the Proxy Statement, with the SEC, pursuant to Regulation 14A, not later than 120 days after the end of our fiscal year. Accordingly, certain information required by Part III has been omitted under General Instruction G(3) to Form 10-K. Only those sections of the 2019 Proxy Statement that specifically address the items set forth herein are incorporated by reference.

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this Item 10 will be included in our Proxy Statement under the captions “Information Regarding the Board of Directors and Corporate Governance,” “Election of Directors,” “Executive Officers” and “Section 16(a) Beneficial Ownership Reporting Compliance” and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this Item 11 will be included in our Proxy Statement under the captions “Executive Compensation” and “Director Compensation” and is incorporated herein by reference.

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

The information required by this Item 12 will be included in our Proxy Statement under the captions “Security Ownership of Certain Beneficial Owners and Management” and “Securities Authorized for Issuance under Equity Compensation Plans” and is incorporated herein by reference.

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

The information required by this Item 13 will be included in our Proxy Statement under the captions “Transactions with Related Persons” and “Independence of the Board of Directors” and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this Item 14 will be included in our Proxy Statement under the caption “Ratification of Selection of Independent Registered Public Accounting Firm” and is incorporated herein by reference.

Item 15. Exhibits, Financial Statement Schedules.

(a)(1) Financial Statements

See the Index to Consolidated Financial Statements in Item 8 of this Annual Report on Form 10-K.

PhaseBio Pharmaceuticals, Inc.

Index to Financial Statements

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Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
PhaseBio Pharmaceuticals, Inc.:

Opinion on the Financial Statements

We have audited the accompanying balance sheets of PhaseBio Pharmaceuticals, Inc. (the Company) as of December 31, 2018 and 2017, the related statements of operations, redeemable convertible preferred stock and stockholders' equity (deficit), and cash flows for the years then ended, and the related notes (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 U.S. generally accepted accounting principles.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. 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/ KPMG LLP

We have served as the Company's auditor since 2010.

Philadelphia, Pennsylvania
March 26, 2019

PHASEBIO PHARMACEUTICALS, INC.
BALANCE SHEETS
(in thousands, except share and per share amounts)

	December 31,	
	2018	2017
Assets		
Current assets:		
Cash and cash equivalents	\$ 61,031	\$ 13,406
Restricted cash	20	20
Other receivable	233	—
Prepaid expenses and other assets	1,344	340
Total current assets	62,628	13,766
Property and equipment, net	355	302
Other assets	43	31
Total assets	<u>\$ 63,026</u>	<u>\$ 14,099</u>
Liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)		
Current liabilities:		
Convertible promissory notes, net of discount	\$ —	\$ 12,095
Derivative liability	—	3,028
Current portion of long-term debt	—	761
Accounts payable	1,806	430
Accrued expenses	2,771	1,281
Total current liabilities	4,577	17,595
Preferred stock warrant liability	—	1,656
Deferred rent	22	5
Long-term debt	7,500	2,625
Total liabilities	12,099	21,881
Commitments and contingencies (<i>Note 7</i>)		
Redeemable convertible preferred stock, \$0.001 par value; zero and 13,321,350 shares authorized at December 31, 2018 and 2017, respectively; zero and 9,131,999 shares issued and outstanding at December 31, 2018 and 2017, respectively.	—	89,634
Stockholders' equity (deficit):		
Preferred stock, \$0.001 par value; 10,000,000 and zero shares authorized at December 31, 2018 and 2017, respectively; zero shares issued and outstanding at December 31, 2018 and 2017, respectively	—	—
Common stock, \$0.001 par value; 200,000,000 and 14,918,087 shares authorized at December 31, 2018 and 2017, respectively; 24,528,242 shares issued and 24,498,275 shares outstanding at December 31, 2018; 775,755 shares issued and 745,788 shares outstanding at December 31, 2017	25	1
Treasury stock, at cost, 29,967 shares as of December 31, 2018 and 2017	(24)	(24)
Additional paid-in capital	173,837	1,672
Accumulated deficit	(122,911)	(99,065)
Total stockholders' equity (deficit)	50,927	(97,416)
Total liabilities, redeemable convertible preferred stock, and stockholders' equity (deficit)	<u>\$ 63,026</u>	<u>\$ 14,099</u>

See accompanying notes to financial statements.

PHASEBIO PHARMACEUTICALS, INC.
STATEMENTS OF OPERATIONS
(in thousands, except share and per share amounts)

	Year Ended December 31,	
	2018	2017
Grant revenues	\$ 668	\$ —
Operating expenses:		
Research and development	15,455	6,210
General and administrative	4,857	2,328
Total operating expenses	20,312	8,538
Loss from operations	(19,644)	(8,538)
Other income (expense):		
Interest income	387	52
Interest expense	(3,924)	(2,723)
Change in fair value of warrant liability	11	1,019
Change in fair value of derivative liability	(676)	(57)
Total other income (expense)	(4,202)	(1,709)
Net loss	\$ (23,846)	\$ (10,247)
Net loss per common share, basic and diluted	\$ (4.49)	\$ (13.78)
Weighted average common shares outstanding, basic and diluted	5,305,062	743,470

See accompanying notes to financial statements.

PHASEBIO PHARMACEUTICALS, INC.
STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
(in thousands, except share amounts)

	Redeemable Convertible Preferred Stock		Stockholders' Equity (Deficit)						Total Stockholders' Equity (Deficit)
			Common Stock		Treasury Stock		Additional Paid-in Capital	Accumulated Deficit	
	Shares	Amount	Shares	Amount	Shares	Amount			Capital
Balance at December 31, 2016	9,131,999	\$ 89,567	773,208	\$ 1	(29,967)	\$ (24)	\$ 1,659	\$ (88,818)	\$ (87,182)
Exercises of stock options	—	—	2,547	—	—	—	3	—	3
Stock-based compensation	—	—	—	—	—	—	77	—	77
Accretion of redeemable preferred stock									
to redemption value	—	67	—	—	—	—	(67)	—	(67)
Net loss	—	—	—	—	—	—	—	(10,247)	(10,247)
Balance at December 31, 2017	9,131,999	89,634	775,755	1	(29,967)	(24)	1,672	(99,065)	(97,416)
Issuance of redeemable preferred stock	1,842,959	14,890	—	—	—	—	—	—	—
Issuance of redeemable preferred stock upon conversion of promissory notes	2,080,209	19,778	—	—	—	—	—	—	—
Exercises of warrants for preferred stock	144,948	1,212	—	—	—	—	—	—	—
Accretion of redeemable preferred stock									
to redemption value	—	95	—	—	—	—	(95)	—	(95)
Conversion of redeemable convertible preferred stock warrants into common stock warrants	—	—	—	—	—	—	3,346	—	3,346
Conversion of redeemable convertible preferred stock into common stock	(13,200,115)	(125,609)	13,225,048	13	—	—	125,596	—	125,609
Issuance of common stock in initial public offering, net	—	—	9,864,666	10	—	—	42,964	—	42,974
Exercises of warrants for common stock, net	—	—	619,086	1	—	—	(70)	—	(69)
Exercises of stock options	—	—	43,687	—	—	—	92	—	92
Stock-based compensation	—	—	—	—	—	—	332	—	332
Net loss	—	—	—	—	—	—	—	(23,846)	(23,846)
Balance at December 31, 2018	<u>—</u>	<u>\$ —</u>	<u>24,528,242</u>	<u>\$ 25</u>	<u>(29,967)</u>	<u>\$ (24)</u>	<u>\$ 173,837</u>	<u>\$ (122,911)</u>	<u>\$ 50,927</u>

See accompanying notes to financial statements.

PHASEBIO PHARMACEUTICALS, INC.
STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,	
	2018	2017
Operating activities		
Net loss	\$ (23,846)	\$ (10,247)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	105	96
Stock-based compensation	332	77
Non-cash interest expense	3,664	2,711
Change in fair value warrant liability	(11)	(1,019)
Change in fair value derivative liability	676	57
Changes in operating assets and liabilities:		
Other receivable	(233)	—
Prepaid expenses and other assets	(1,017)	40
Accounts payable	1,337	(213)
Accrued expenses	1,923	242
Deferred rent	17	(3)
Net cash used in operating activities	<u>(17,053)</u>	<u>(8,259)</u>
Investing activities		
Purchases of property and equipment	(119)	(216)
Net cash used in investing activities	<u>(119)</u>	<u>(216)</u>
Financing activities		
Proceeds from issuance of common stock in initial public offering, net	42,974	—
Proceeds from issuance of redeemable convertible preferred stock, net	17,712	—
Proceeds from term loan, net	3,995	3,480
Proceeds from exercise of stock options	92	3
Proceeds from exercise of warrants	24	—
Proceeds from convertible promissory notes, net	—	14,683
Net cash provided by financing activities	<u>64,797</u>	<u>18,166</u>
Net increase in cash and cash equivalents	47,625	9,691
Cash, cash equivalents and restricted cash at the beginning of the year	13,426	3,735
Cash, cash equivalents and restricted cash at the end of the year	<u>\$ 61,051</u>	<u>\$ 13,426</u>
Supplemental disclosure for cash flow		
Cash paid for interest	<u>\$ 260</u>	<u>\$ 12</u>
Supplemental disclosure of cash flow information		
Conversion of redeemable convertible preferred stock into common stock	<u>\$ 125,609</u>	<u>\$ —</u>
Conversion of convertible promissory notes into redeemable convertible preferred stock	<u>\$ 19,778</u>	<u>\$ —</u>
Warrant liability converted to redeemable convertible preferred stock upon the exercise of warrants	<u>\$ 4,297</u>	<u>\$ —</u>
Issuance of warrants in conjunction with debt	<u>\$ 2,822</u>	<u>\$ 1,795</u>
Conversion of redeemable convertible preferred stock warrants into common stock warrants	<u>\$ 3,346</u>	<u>\$ —</u>
Accretion of redeemable convertible preferred stock	<u>\$ 95</u>	<u>\$ 67</u>
Purchases of property and equipment included in accounts payable	<u>\$ 39</u>	<u>\$ —</u>
Issuance of derivative in conjunction with debt	<u>\$ —</u>	<u>\$ 2,971</u>

See accompanying notes to financial statements.

PHASEBIO PHARMACEUTICALS INC.
NOTES TO THE FINANCIAL STATEMENTS

1. Organization and Description of Business

Description of Business

PhaseBio Pharmaceuticals, Inc. (the “Company”) was incorporated as a Delaware corporation on January 10, 2002. The Company is a clinical-stage biopharmaceutical company focused on the development and commercialization of novel therapies to treat orphan diseases, with an initial focus on cardiopulmonary indications. The Company’s lead product candidate, PB2452, is a novel reversal agent for the antiplatelet drug ticagrelor, which the Company is developing for the treatment of patients on ticagrelor who are experiencing a major bleeding event or those who require urgent surgery. The Company recently completed a Phase 1 clinical trial of PB2452 in healthy subjects and intends to initiate a Phase 2a clinical trial in healthy older subjects in the first half of 2019. The Company’s second product candidate, PB1046, is a once-weekly fusion protein currently in a Phase 2b clinical trial for the treatment of pulmonary arterial hypertension. PB1046 utilizes the Company’s proprietary half-life extending elastin-like polypeptide (“ELP”), technology, which also serves as the engine for future product pipeline candidates.

Initial Public Offering

On October 22, 2018, the Company completed an initial public offering (“IPO”) of its common stock, which resulted in the issuance and sale of an aggregate of 9,864,666 shares of common stock at a public offering price of \$5.00 per share, generating net proceeds of approximately \$43.0 million after deducting underwriting discounts and commissions and other offering costs. In connection with the completion of the IPO, all then-outstanding shares of the Company’s redeemable convertible preferred stock were converted into an aggregate of 13,200,115 shares of common stock.

Upon completion of the IPO, the Company’s certificate of incorporation was amended and restated. Under the amended and restated certificate of incorporation, the Company’s authorized capital stock consists of 200,000,000 shares of common stock with a par value of \$0.001 per share and 10,000,000 shares of preferred stock with a par value of \$0.001 per share.

Reverse Stock Split

In October 2018, the Company effected a 11.0634-for-1 reverse split of its outstanding common stock and redeemable convertible preferred stock. No fractional shares were issued in connection with the stock split, and the par value and other terms of the common stock were not affected by the stock split. All share and per share amounts, including stock options, have been retroactively adjusted in these financial statements for all periods presented to reflect the reverse stock split. Further, exercise prices of stock options have been retroactively adjusted in these financial statements for all periods presented to reflect the reverse stock split.

Liquidity

The Company has experienced net losses and negative cash flows from operations since its inception and, as of December 31, 2018, had an accumulated deficit of \$122.9 million. The Company expects to continue to incur net losses for at least the next several years. As of December 31, 2018, the Company had cash and cash equivalents of \$61.0 million and working capital of \$58.1 million. The Company believes that its existing cash and cash equivalents are sufficient to fund its operating expenses and capital requirements into the second quarter of 2020.

Basis of Presentation

The accompanying financial statements have been prepared in accordance with U.S. generally accepted accounting principles (“GAAP”) and the rules and regulations of the Securities and Exchange Commission (“SEC”). Any reference in these notes to applicable guidance is meant to refer to GAAP as found in the Accounting Standards Codification (“ASC”) and Accounting Standards Updates (“ASU”) promulgated by the Financial Accounting Standards Board (“FASB”). Certain non-significant reclassifications have been made to conform the prior period presentation.

The Company manages its operations as a single reportable segment for the purposes of assessing performance and making operating decisions.

2. Significant Accounting Policies

Use of Estimates

The preparation of the Company’s financial statements requires management to make estimates and assumptions that impact the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in the Company’s financial statements and accompanying notes. The most significant estimates in the Company’s financial statements relate to the valuation of redeemable convertible preferred stock warrants prior to the IPO, the conversion option on the convertible notes and clinical trial accruals. Although these estimates are based on the Company’s knowledge of current events and actions it may undertake in the future, actual results could differ materially from those estimates and assumptions.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist primarily of cash and cash equivalents. The Company maintains certain deposits in federally insured financial institutions in excess of federally insured limits. The Company could experience losses on the money market funds in the future.

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity from the date of purchase of three months or less to be cash equivalents. Cash and cash equivalents include cash in readily available checking and money market accounts.

Restricted Cash

The Company had restricted cash of \$20,000 as of December 31, 2018 and 2017, which was held in a certificate of deposit at the Company’s bank to secure the Company’s corporate credit card.

Fair Value of Financial Instruments

The carrying amounts of accounts receivable, prepaid expenses and other current assets, accounts payable and accrued expenses are reasonable estimates of their fair value because of the short maturity of these items. Based on the borrowing rates currently available to the Company for loans with similar terms, the Company believes the fair value of the term loan approximates its carrying value (see Note 6).

Property and Equipment

Property and equipment are recorded at cost and depreciated over the estimated useful lives of the assets (three to five years) using the straight-line method. Leasehold improvements are amortized over the shorter of their estimated useful lives or the lease term.

Long-Lived Assets

The Company regularly reviews the carrying value and estimated lives of all of its long-lived assets, including property and equipment to determine whether indicators of impairment may exist which warrant adjustments to carrying values or estimated useful lives. The determinants used for this evaluation include management's estimate of the asset's ability to generate net positive cash flow in future periods as well as the strategic significance of the assets to the Company's business objective. Should an impairment exist, the impairment loss would be measured based on the extent that the estimated fair value is less than its carrying value. The Company has not recognized any impairment losses in the years ended December 31, 2018 and 2017.

Preferred Stock Warrant Liability

The Company previously issued freestanding warrants to purchase shares of its redeemable convertible preferred stock. Since the underlying redeemable convertible preferred stock was classified outside of permanent equity, those warrants were classified as liabilities in the accompanying balance sheet. Warrants classified as liabilities were recorded at their estimated fair value on the date of issuance and were revalued at each subsequent balance sheet date, with fair value changes recognized as increases or reductions to other income (expense) in the accompanying statements of operations. The Company estimated the fair value of these warrants using the Black-Scholes option pricing model.

In connection with the Company's IPO in October 2018, all warrants were either exercised or converted into warrants to purchase common stock, at which time the liability was reclassified to stockholders' equity.

Preclinical and Clinical Trial Accruals

The Company accrues and expenses preclinical studies and clinical trial activities performed by third parties based upon estimates of the proportion of work completed over the life of the individual trial and subject enrollment rates in accordance with agreements with clinical research organizations and clinical trial sites. The Company determines the estimates by reviewing contracts, vendor agreements and purchase orders, and through discussions with internal clinical personnel and external service providers as to the progress or stage of completion of trials or services and the agreed-upon fee to be paid for such services. However, actual costs and timing of clinical trials are highly uncertain, subject to risks and may change depending upon a number of factors, including the Company's clinical development plan.

Management makes estimates of the Company's accrued expenses as of each balance sheet date in the Company's financial statements based on facts and circumstances known to the Company at that time. If the actual timing of the performance of services or the level of effort varies from the estimate, the Company will adjust the accrual accordingly. Nonrefundable advance payments for goods and services, including fees for process development or manufacturing and distribution of clinical supplies that will be used in future research and development activities, are deferred and recognized as expense in the period that the related goods are consumed or services are performed.

Research and Development Expense

Research and development costs are expensed as incurred.

Stock-Based Compensation

The Company measures and recognizes compensation expense for all stock-based compensation based on the estimated fair value at the date of grant. Currently, the Company's stock-based awards consist only of stock options; however, future grants under the Company's equity compensation plan may also consist of shares of restricted stock, restricted stock units, stock appreciation rights, performance awards and performance units. The Company estimates the fair value of stock options using the Black-Scholes option-pricing model, which requires the use of estimates.

The Company recognizes stock-based compensation cost for ratably vesting stock options on a straight-line basis over the requisite service period of the award.

The Black-Scholes option-pricing model requires the input of subjective assumptions, including the risk-free interest rate, the fair value of the underlying common stock prior to the IPO, the expected dividend yield of the Company's common stock, the expected volatility of the price of the Company's common stock, and the expected term of the option. These estimates involve inherent uncertainties and the application of management's judgment. If factors change and different assumptions are used, the Company's stock-based compensation expense could be materially different in the future.

Income Taxes

The Company accounts for income taxes under the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements. Under this method, deferred tax assets and liabilities are determined on the basis of the differences between the financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. The effect of a change in tax rates on deferred tax assets and liabilities is recognized in income in the period that includes the enactment date.

The Company recognizes net deferred tax assets to the extent that the Company believes these assets are more likely than not to be realized. In making such a determination, management considers all available positive and negative evidence, including future reversals of existing taxable temporary differences, projected future taxable income, tax-planning strategies, and results of recent operations. If management determines that the Company would be able to realize its deferred tax assets in the future in excess of their net recorded amount, management would make an adjustment to the deferred tax asset valuation allowance, which would reduce the provision for income taxes.

The Company records uncertain tax positions on the basis of a two-step process whereby (1) management determines whether it is more likely than not that the tax positions will be sustained on the basis of the technical merits of the position and (2) for those tax positions that meet the more-likely-than-not recognition threshold, management recognizes the largest amount of tax benefit that is more than 50% likely to be realized upon ultimate settlement with the related tax authority. The Company recognizes interest and penalties related to unrecognized tax benefits, if any, within income tax expense, and any accrued interest and penalties are included within the related tax liability line.

Grant Revenues

Grant revenues are derived from government grants that support the Company's efforts on specific research projects. The Company has determined that the government agencies providing grants to the Company are not customers. The Company recognizes grant revenue when there is reasonable assurance of compliance with the conditions of the grant and reasonable assurance that the grant revenue will be received.

Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss by the weighted average number of common shares outstanding during the period. Diluted net loss per share is computed by dividing the net loss by the weighted average number of common shares and common share equivalents outstanding for the period. Common stock equivalents are only included when their effect is dilutive. The Company's potentially dilutive securities which include redeemable convertible preferred stock, warrants and outstanding stock options under the Company's stock option plan have been excluded from the computation of diluted net loss per share as they would be anti-dilutive. For all periods presented, there is no difference in the number of shares used to compute basic and diluted shares outstanding due to the Company's net loss position.

The following table sets forth the outstanding potentially dilutive securities that have been excluded in the calculation of diluted net loss per share because their inclusion would be anti-dilutive.

	<u>As of December 31,</u>	
	<u>2018</u>	<u>2017</u>
Common stock options	1,545,403	1,075,209
Warrants to purchase common stock	75,597	—
Redeemable convertible preferred stock	—	9,131,999
Warrants to purchase redeemable convertible preferred stock	—	486,356
Total	<u>1,621,000</u>	<u>10,693,564</u>

Recent Accounting Pronouncements

In February 2016, the FASB issued ASU No. 2016-02, *Leases*. This update amends the current accounting guidance for lease transactions. Under the new guidance, a lessee will be required to recognize both assets and liabilities for any leases in excess of twelve months. Additionally, certain qualitative and quantitative disclosures will also be required in the financial statements. This guidance will be effective for public companies for annual and interim periods beginning after December 15, 2018. The Company will adopt ASU 2016-02 in 2019. Upon adoption, the Company expects to record a right of use asset and a corresponding lease liability of an amount between \$1.5 million and \$2.5 million.

In August 2016, the FASB issued ASU No. 2016-15, *Classification of Certain Cash Receipts and Cash Payments (Topic 230)*. ASU 2016-15 addresses eight specific cash flow issues with the objective of reducing the existing diversity in practice for certain cash receipts and cash payments. The Company adopted this standard in the first quarter of 2018, and the adoption did not have any impact on the Company's financial statements.

In May 2017, the FASB issued ASU No. 2017-09, *Compensation—Stock Compensation (Topic 718): Scope of Modification Accounting*, which clarifies when to account for a change to the terms or conditions of a share-based payment award as a modification. Under the new guidance, modification accounting is required only if the fair value, the vesting conditions, or the classification of the award (as equity or liability) changes as a result of the change in terms or conditions. The Company adopted this guidance effective January 1, 2018, and the adoption did not have a material impact on the Company's financial statements.

In June 2018, the FASB issued ASU 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting*, which largely aligns the accounting for share-based payment awards issued to nonemployees with the accounting for share-based payment awards issued to employees. Under previous GAAP, the accounting for nonemployee share-based payments differed from that applied to employee awards, particularly with regard to the measurement date and the impact of performance conditions. Under the new guidance, (1) equity-classified share-based payment awards issued to nonemployees will be measured at the grant date, instead of the previous requirement to remeasure the awards through the performance completion date, (2) for performance conditions, compensation cost associated with the award will be recognized when the achievement of the performance condition is probable, rather than upon achievement of the performance condition and (3) the current requirement to reassess the classification (equity or liability) for nonemployee awards upon vesting will be eliminated, except for awards in the form of convertible instruments. The Company adopted this standard effective October 1, 2018, and the adoption did not have a material impact on the Company's financial statements.

In August 2018, the FASB issued ASU 2018-13, *Fair Value Measurement - Disclosure Framework (Topic 820): Changes to the Disclosure Requirements for Fair Value Measurement*. The updated guidance improves the disclosure requirements on fair value measurements. The updated guidance is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. Early adoption is permitted for any removed or modified disclosures. The Company is currently assessing the timing and impact of adopting the updated provisions.

3. Fair Value Measurement

Fair value is defined as an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or a liability.

The Company classifies fair value measurements in one of the following three categories for disclosure purposes:

Level 1: Quoted prices in active markets for identical assets or liabilities.

Level 2: Inputs other than Level 1 prices for similar assets or liabilities that are directly or indirectly observable in the marketplace.

Level 3: Unobservable inputs which are supported by little or no market activity and values determined using pricing models, discounted cash flow methodologies, or similar techniques, as well as instruments for which the determination of fair value requires significant judgment or estimation.

The Company's cash equivalents are classified using Level 1 inputs within the fair value hierarchy because they are valued using quoted market prices, broker or dealer quotations, or alternative pricing sources with reasonable levels of price transparency. None of the Company's non-financial assets or liabilities are recorded at fair value on a non-recurring basis. No transfers between levels have occurred during the periods presented.

The Company estimated the fair value of redeemable convertible preferred stock warrants at the time of issuance and subsequent remeasurement using the Black-Scholes option pricing model at each reporting date, based on the following inputs: the risk-free interest rate; the expected dividend rate; the remaining contractual life of the warrants; the fair value of the underlying stock; and the expected volatility of the price of the underlying common stock. The estimates were based, in part, on subjective assumptions.

The following table summarizes the Company's assets and liabilities that require fair value measurements on a recurring basis and their respective input levels based on the fair value hierarchy (in thousands):

	Fair Value Measurements at Reporting Date			
	Total	Level 1	Level 2	Level 3
As of December 31, 2018:				
Assets				
Cash equivalents	\$ 59,357	\$ 59,357	\$ —	\$ —
As of December 31, 2017:				
Assets				
Cash equivalents	\$ 12,472	\$ 12,472	\$ —	\$ —
Liabilities				
Derivative liability	\$ 3,028	\$ —	\$ —	\$ 3,028
Preferred stock warrant liability	1,656	—	—	1,656
Total liabilities	\$ 4,684	\$ —	\$ —	\$ 4,684

The following weighted-average assumptions were used in determining the fair value of the preferred stock warrant liability valued using the Black-Scholes option pricing model as of December 31, 2017:

	December 31, 2017
Expected volatility	68.0%
Risk-free interest rate	2.2%
Contractual term (in years)	5.9
Expected dividend yield	—

The following estimated fair values per share of the Company's underlying redeemable convertible preferred stock were used to determine the estimated fair value of the preferred stock warrant liability:

	December 31, 2017
Series AA	\$ 5.75
Series B	\$ 3.76
Series C-1	\$ 3.76

The following tables present activity for the preferred stock warrant liability and the derivative liability measured at fair value using significant unobservable Level 3 inputs during the year ended December 31, 2017 and 2018 (in thousands):

	Preferred Stock Warrant Liability
Balance at December 31, 2016	\$ 880
Issuance of warrants	1,795
Changes in fair value reflected as change in fair value of warrant liability	(1,019)
Balance at December 31, 2017	1,656
Issuance of warrants	2,822
Exercise of warrants	(1,197)
Changes in fair value reflected as change in fair value of warrant liability	(11)
Conversion to common stock warrants upon IPO	(3,270)
Balance at December 31, 2018	\$ —

	Derivative Liability
Balance at December 31, 2016	\$ —
Issuance of derivative	2,971
Changes in fair value reflected as change in fair value of derivative liability	57
Balance at December 31, 2017	3,028
Changes in fair value reflected as change in fair value of derivative liability	676
Extinguishment of derivative upon conversion of convertible promissory notes	(3,704)
Balance at December 31, 2018	\$ —

4. Property and Equipment

The following table presents the composition of property and equipment, net as of December 31, 2018 and 2017 (in thousands):

	As of December 31,	
	2018	2017
Lab equipment	\$ 1,764	\$ 1,681
Computer hardware, software and telephone	228	174
Furniture and fixtures	98	70
Leasehold improvements	50	22
	2,140	1,947
Less accumulated depreciation	(1,785)	(1,645)
Property and equipment, net	\$ 355	\$ 302

5. Accrued Expenses

The following table presents the composition of accrued expenses as of December 31, 2018 and 2017 (in thousands):

	As of December 31,	
	2018	2017
Accrued clinical and related costs	\$ 1,358	\$ 197
Accrued compensation and related costs	914	346
Accrued interest	194	628
Accrued other	305	110
Accrued expenses	\$ 2,771	\$ 1,281

6. Debt

Convertible Promissory Notes

In January 2017 and October 2017, the Company issued \$14.7 million of convertible promissory notes (the “2017 Notes”) to holders of Series C-1 redeemable convertible preferred stock (“Series C-1”). The 2017 Notes bore interest at the rate of 8% per annum. Upon a subsequent equity financing of at least \$10.0 million prior to the stated maturity date, the 2017 Notes plus accrued interest would automatically convert into shares of the stock issued by the Company in such financing at a price equal to 80% of the lowest issue price.

The 2017 Notes could have converted into a variable number of shares of preferred stock, and accordingly, the Company determined the conversion provision to be a redemption feature. The redemption feature was evaluated as an embedded derivative and bifurcated from the convertible promissory notes due to the substantial premium paid upon redemption and accounted for as a derivative instrument. Upon bifurcating the redemption feature, the Company recorded a debt discount of \$3.0 million that was recognized in interest expense over the term of the 2017 Notes.

In connection with the 2017 Notes, the Company issued warrants to the noteholders to purchase 304,397 shares of Series C-1. The warrants were exercisable for \$0.12 per share and would expire upon the earlier of (1) the date of the initial closing of a liquidation event, as defined, (2) the closing of a firm commitment underwritten initial public offering or (3) January 2024. All warrants were exercised in connection with the closing of the Company’s IPO. The Company recorded a debt discount of \$1.7 million, which represents the estimated fair value of the warrants, upon issuance of the 2017 Notes, which was being amortized to interest expense over the term of the 2017 Notes using the effective-interest method.

In August 2018, the Company sold 1,842,959 shares of Series D redeemable preferred stock (“Series D”) to new and existing investors at a price of \$9.659 per share for net proceeds of \$17.7 million and issued warrants to purchase 368,582 shares of Series C-1 at an exercise price of \$0.12 per share (the “Series D Financing”). Concurrent with the Series D Financing, all of the Company’s previously outstanding 2017 Notes, including accrued interest thereon, were converted into 2,080,209 shares of Series D.

Interest expense, including the debt discount related to the 2017 Notes, was \$3.4 million and \$2.7 million for the years ended December 31, 2018 and 2017, respectively.

Term Loan

In October 2017, the Company entered into a Loan and Security Agreement (“SVB Loan”) with Silicon Valley Bank (“SVB”), pursuant to which the Company could borrow up to \$7.5 million, issuable in three separate tranches (“Growth Capital Advances”) of \$3.5 million (“Tranche A”), \$2.0 million (“Tranche B”) and \$2.0 million (“Tranche C”). Each of the Growth Capital Advances would become available upon the achievement of certain clinical and regulatory milestones. Under the original terms of the SVB Loan, the Company was to make interest-only payments through June 30, 2018 at a rate equal to the Prime Rate as defined per the SVB Loan. The interest-only period would be extended to December 31, 2018 if the Company borrowed the remaining tranches, followed by an amortization period of 24 months of equal monthly payments of principal plus interest amounts until paid in full. In connection with the SVB Loan, the Company issued to SVB a warrant to purchase 49,713 shares of Series C-1 at an exercise price of \$9.659 per share. The warrant is immediately exercisable and expires on October 18, 2027. The Company was required to make a final payment equal to 7% of the original aggregate principal amount of the Growth Capital Advances at maturity. In November 2017, the Company drew \$3.5 million from Tranche A.

The Company had the option to prepay all, but not less than all, of the borrowed amounts, provided that the Company would have been obligated to pay a prepayment fee equal to (a) 3.0% of the outstanding principal balance of the applicable Growth Capital Advances if prepayment was made prior to the first anniversary of the effective date of the SVB Loan, (b) 2.0% of the outstanding principal balance of the applicable Growth Capital Advances if prepayment was made by the second anniversary of the effective date of the SVB Loan or (c) 1.0% of the outstanding principal balance of the applicable Growth Capital Advances if prepayment was made after the second anniversary of the effective date of the SVB Loan.

In April 2018, the SVB Loan was amended to extend the draw period of Tranche B and Tranche C to April 30, 2018 and July 31, 2018, respectively, as well as to extend the interest-only period through July 31, 2018, which would be extended to December 31, 2018 if the Company borrowed Tranche B and Tranche C. Additionally, all Capital Growth Advances would mature on June 1, 2020; however, if the Company were to draw Tranche B and Tranche C, the maturity date would be December 31, 2020. On April 30, 2018, the Company borrowed \$2.0 million under Tranche B.

In July 2018, the SVB Loan was amended to further extend the draw period of Tranche C to August 31, 2018, as well as to extend the interest-only period of the SVB Loan through August 31, 2018, which would be extended to December 31, 2018 if the Company were to draw Tranche C. In August 2018, the Company borrowed \$2.0 million under Tranche C.

The Company’s obligations under the SVB Loan are secured by a first priority security interest in substantially all of its current and future assets, other than its owned intellectual property. The Company is also obligated to comply with various other customary covenants, including restrictions on its ability to encumber intellectual property assets.

The Company recorded a debt discount of \$0.4 million for the estimated fair value of warrants and debt issuance costs upon the borrowing of Tranche A and Tranche B, which is being amortized to interest expense over the term of the SVB Loan using the effective-interest method. As of December 31, 2018 and 2017, the Company had \$7.5 million and \$3.5 million, respectively, of outstanding principal under the SVB Loan and \$7.5 million and \$3.4 million, respectively, is reflected on the balance sheet net of debt discounts. Interest expense, including amortization of debt discount related to the term debt, totaled \$0.6 million and \$0.1 million for the years ended December 31, 2018 and 2017, respectively. The Company was in compliance with all covenants under the SVB Loan as of December 31, 2018.

On March 25, 2019, the Company repaid the outstanding principal balance and accrued portion of the final payment for the SVB Loan in full (see Note 15). The following table sets forth by year the Company's required future principal payments for the refinanced SVB Loan (in thousands):

<u>Years Ending December 31,</u>	
2019	\$ —
2020	2,142
2021	2,285
2022	2,438
2023	635
Thereafter	—
	<u>\$ 7,500</u>

7. Commitments and Contingencies

Operating Leases

The Company leases office and research and development facilities and equipment under various non-cancellable operating lease agreements. In January 2010, the Company entered into a lease for office and laboratory space in Malvern, Pennsylvania (the "Malvern Lease"). The Malvern Lease commenced in March 2010 and was amended to extend its term to September 30, 2023. This lease contains escalating rent payments. In December 2018, the Company entered into a lease for office space in San Diego, California, which expires in October 2022.

The Company's future minimum commitments under its non-cancelable operating leases were as follows (in thousands):

<u>Year Ending December 31,</u>	
2019	\$ 342
2020	368
2021	373
2022	360
2023	204
Thereafter	—
Total	<u>\$ 1,647</u>

The Company recognizes rent expense for the facility operating leases on a straight-line basis. The Company accounts for the difference between the minimum lease payments and the straight-line amount as deferred rent. Rent expense was \$0.4 million for the years ended December 31, 2018 and 2017.

Legal Proceedings

The Company is not currently a party to any litigation, nor is management aware of any pending or threatened litigation against the Company, that it believes would materially affect the Company's business, operating results, financial condition or cash flows.

Supply Agreement

The Company has entered into a Master Services Agreement (“Supply Agreement”) with BioVectra Inc., (“BioVectra”). BioVectra will manufacture and supply cGMP-grade quantities of the Company’s PB2452 proprietary drug product (“Product”) for the Company’s potential PB2452 Phase 3 clinical trial as well as any work required to support the marketing authorization filing. A Commercial Supply Agreement is being put in place for the Product, if it is approved by the FDA.

BioVectra is responsible for the facility, including performing all work related to the procurement, design, project management, installation, assembly, commissioning and validation of the facility and all equipment, and for financing all costs associated with building out the facility. The Company will be responsible for the purchase of certain equipment and raw materials for the production process.

8. Preferred Stock Warrants

The Company accounted for its warrants to purchase shares of redeemable convertible preferred stock as liabilities as they were exercisable for a redeemable instrument. The Company continued to adjust the liability for changes in fair value of these warrants until they were exercised or converted to common stock warrants.

The following table summarizes the outstanding redeemable convertible preferred stock warrants and the corresponding exercise price as of December 31, 2017:

	<u>Number of Shares Outstanding as of December 31, 2017</u>	<u>Exercise Price</u>	<u>Expiration Date</u>
Series AA warrants	1,506	\$ 13.28	March 7, 2018
2009 Series B warrants	25,884	\$ 9.659	December 22, 2019
2014 Series B warrants	104,856	\$ 0.12	May 14, 2021
Convertible debt Series C-1 warrants	304,397	\$ 0.12	January 17, 2024
Term loan Series C-1 warrants	49,713	\$ 9.659	October 18, 2027
	<u>486,356</u>		

In August 2018, as part of the Series D Financing, the Company issued warrants to purchase 368,582 shares of Series C-1 redeemable convertible preferred stock (the “2018 Series C-1 warrants”) at an exercise price of \$0.12 per share.

In connection with the IPO in October 2018, all outstanding redeemable convertible preferred stock warrants were either exercised or converted to common stock warrants. During 2018, stockholders exercised the outstanding 2014 Series B warrants, convertible debt Series C-1 warrants and the 2018 Series C-1 warrants to purchase an aggregate of 764,034 shares of the Company’s redeemable convertible preferred stock and common stock, at a weighted-average exercise price of \$0.12 per share. The outstanding 2009 Series B warrants and Term loan Series C-1 warrants were automatically converted into an aggregate of 75,597 common stock warrants, to which the liability was reclassified to stockholders’ equity.

9. Redeemable Convertible Preferred Stock and Stockholders’ Deficit

Preferred Stock

The Company issued Series 1 redeemable convertible preferred stock (“Series 1”), Series 2 redeemable preferred stock (“Series 2”), Series AA redeemable convertible preferred stock (“Series AA”), Series B redeemable convertible preferred stock (“Series B”), Series C-1, Series C-2 redeemable convertible preferred stock (“Series C-2”), Series C-3 redeemable convertible preferred stock (“Series C-3”), and Series D (collectively, “Preferred Stock”). Upon the closing of the IPO on October 22, 2018, all shares of Preferred Stock were automatically converted into an aggregate of 13,200,115 shares of common stock.

As of December 31, 2017, the authorized, issued, and outstanding shares of Preferred Stock and their carrying amounts and liquidation values were as follows:

	<u>Shares Authorized</u>	<u>Shares Issued and Outstanding</u>	<u>Carrying Amount</u>	<u>Liquidation Value</u>
Series 1	132,255	132,255	\$ 522,266	\$ 526,778
Series 2	1	1	240,242	250,000
Series AA	575,470	573,961	7,615,583	7,619,998
Series B	6,382,259	6,251,502	60,366,480	60,379,282
Series C-1	4,524,375	2,174,280	20,888,972	20,999,997
Series C-2	916,095	—	—	—
Series C-3	790,895	—	—	—
Total	<u>13,321,350</u>	<u>9,131,999</u>	<u>\$ 89,633,543</u>	<u>\$ 89,776,055</u>

Conversion

All shares of Preferred Stock were automatically converted into an aggregate of 13,200,115 shares of common stock upon the closing of the IPO on October 22, 2018.

10. Stock-Based Compensation

Stock Plans

In July 2018, the Company amended the Company's Amended and Restated 2002 Stock Plan (the "2002 Plan") to reserve an additional 800,000 shares of common stock for issuance under the 2002 Plan.

In October 2018, the Company's board of directors and stockholders adopted and approved the 2018 Equity Incentive Plan (the "2018 Plan"), which is a successor to and continuation of the 2002 Plan. The 2018 Plan became effective upon the execution of the underwriting agreement related to the IPO on October 17, 2018. No further grants will be made under the 2002 Plan.

Initially, the maximum number of shares of the Company's common stock that may be issued under the 2018 Plan is 3,231,626 shares. As of December 31, 2018, the Company had 1,670,921 shares available for grant under the 2018 Plan. The number of shares of common stock reserved for issuance under the 2018 Plan will automatically increase on January 1 of each calendar year, starting on January 1, 2019 through January 1, 2028, in an amount equal to 3% of the total number of shares of the Company's capital stock outstanding on the last day of the calendar month before the date of each automatic increase, or a lesser number of shares determined by the Company's board of directors. Subject to this provision, the Company added 734,948 shares available for grant to the 2018 Plan effective January 1, 2019. The maximum number of shares of the Company's common stock that may be issued on the exercise of incentive stock options under the 2018 Plan is 9,694,878.

The following table summarizes stock option activity for the 2002 Plan and 2018 Plan for the year ended December 31, 2018:

	Total Options	Weighted- Average Exercise Price Per Share	Weighted- Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Outstanding at Ended December 31, 2016	1,001,546	\$ 1.62	8.1	\$ 58,619
Granted	99,866	\$ 1.44		
Exercised	(2,547)	\$ 1.20		
Cancelled or expired	(23,656)	\$ 1.76		
Outstanding at December 31, 2017	1,075,209	\$ 1.60	7.3	\$ 711,328
Granted	563,268	\$ 4.07		
Exercised	(43,687)	\$ 2.12		
Cancelled or expired	(49,387)	\$ 1.65		
Outstanding at December 31, 2018	1,545,403	\$ 2.48	7.6	\$ 1,593,487
Vested and expected to vest at December 31, 2018	1,545,403	\$ 2.48	7.6	\$ 1,593,487
Vested and exercisable at December 31, 2018	801,294	\$ 1.65	6.3	\$ 1,175,200

The weighted-average grant date fair value per share of options granted was \$2.75 and \$1.00 for the years ended December 31, 2018 and 2017, respectively. The aggregate intrinsic value of options exercised was \$0.2 million and \$686 for the years ended December 31, 2018 and 2017, respectively.

As of December 31, 2018, the total unrecognized compensation expense related to unvested employee and non-employee stock option awards was \$1.6 million, which was expected to be recognized in expense over a weighted-average period of approximately 2.9 years.

In October 2018, the Company's board of directors and stockholders approved the 2018 Employee Stock Purchase Plan (the "ESPP"). The ESPP became effective on October 17, 2018. The purpose of the ESPP is to secure the services of new employees, to retain the services of existing employees and to provide incentives for such individuals to exert maximum efforts toward the Company's success and that of the Company's affiliates. The ESPP is intended to qualify as an "employee stock purchase plan" within the meaning of Section 423 of the Code for U.S. employees.

The ESPP authorizes the issuance of 196,000 shares of the Company's common stock under purchase rights granted to the Company's employees or to employees of any of the Company's designated affiliates. The number of shares of common stock reserved for issuance will automatically increase on January 1 of each calendar year, beginning on January 1, 2019 through January 1, 2028, by the lesser of (1) 1% of the total number of shares of the Company's common stock outstanding on the last day of the calendar month before the date of the automatic increase, and (2) 490,000 shares; provided that before the date of any such increase, the Company's board of directors may determine that such increase will be less than the amount set forth in clauses (1) and (2). Subject to this provision, the Company added 244,983 shares available for grant to the ESPP effective January 1, 2019. As of December 31, 2018, no shares of common stock have been purchased under the ESPP.

Determining Fair Value of Stock Options

The fair value of each grant of stock options was determined by the Company using the methods and assumptions discussed below. Certain of these inputs are subjective and generally require judgment to determine.

Expected Term—The expected term of stock options represents the weighted average period the stock options are expected to be outstanding. The Company uses the simplified method for estimating the expected term. The simplified method calculates the expected term as the average time-to-vesting and the contractual life of the options.

Expected Volatility—Due to the Company’s limited operating history and lack of company-specific historical or implied volatility, the expected volatility assumption was determined by examining the historical volatilities of a group of industry peers whose share prices are publicly available.

Risk-Free Interest Rate—The risk-free rate assumption is based on the U.S. Treasury instruments, the terms of which were consistent with the expected term of the Company’s stock options.

Expected Dividend—The Company has not paid and does not intend to pay dividends.

Common Stock Valuation—Due to the absence of a public market trading the Company’s common stock prior to the IPO, it was necessary to estimate the fair value of the common stock underlying the stock-based grants when performing fair value calculations using the Black-Scholes option pricing model. The fair value of the common stock underlying the stock-based grants was assessed for each grant date by the board of directors. All options to purchase shares of common stock have been granted with an exercise price per share no less than the fair value per share of the common stock underlying those options on the date of grant.

In the absence of a public trading market for the Company’s common stock, the Company determined the estimated fair value of its common stock using methodologies, approaches, and assumptions consistent with the American Institute of Certified Public Accountants (“AICPA”) Audit and Accounting Practice Aid Series: Valuation of Privately Held Company Equity Securities Issued as Compensation (“AICPA Practice Aid”).

The fair value of each option was estimated on the date of grant using the weighted average assumptions in the table below:

	Year Ended December 31,	
	2018	2017
Risk-free interest rate	2.88%	2.88%
Expected term (in years)	7.0	7.1
Expected volatility	69%	68%
Expected dividend yield	—	—
Estimated fair value of common stock	\$ 4.07	\$ 1.00

Stock-based compensation expense has been reported in the Company’s statements of operations for the years ended December 31, 2018 and 2017 as follows (in thousands):

	Year Ended December 31,	
	2018	2017
General and administrative	\$ 208	\$ 40
Research and development	124	37
Total stock-based compensation	\$ 332	\$ 77

11. License Agreements

MedImmune Limited

In November 2017, the Company entered into a license agreement (“MedImmune License”) with MedImmune Limited (“MedImmune”). MedImmune is a wholly owned subsidiary of AstraZeneca plc. Pursuant to the terms of the MedImmune License, MedImmune granted the Company exclusive global rights for the purpose of developing and commercializing products under the MedImmune License (“MedImmune licensed product”). In consideration of the license and other rights granted by MedImmune, the Company made an upfront payment of \$0.1 million, which was included as research and development expense for the year ended December 31, 2017. The Company is also obligated to make a series of contingent milestone payments totaling up to an aggregate of \$18.0 million upon the achievement of clinical development and regulatory milestones. As of December 31, 2018, none of the clinical development or regulatory filing milestones had been met. In addition, the Company will pay MedImmune tiered

royalties ranging from mid-single-digit to low-teen percentages of net sales of any MedImmune licensed products and additional payments of up to \$50.0 million in aggregate commercial milestones. The Company also must pay quarterly fees relating to technical services provided by MedImmune. The MedImmune License requires the Company to cooperate with MedImmune on commercial messaging of PB2452 and provides MedImmune with the return of rights to PB2452 if certain commercial diligence requirements are not achieved by the Company. In addition, the MedImmune License offers an option for third-party product storage costs. As of December 31, 2017, the Company had incurred and reimbursed MedImmune \$0.5 million for such third-party product storage costs. The Company incurred an insignificant amount of third-party product storage costs in the year ended December 31, 2018. AstraZeneca plc is a stockholder of the Company.

Duke University

In October 2006, the Company entered into a license agreement with Duke University (“Duke”) (as amended, the “Duke License”). Pursuant to the Duke License, Duke granted to the Company an exclusive, worldwide license under certain patent rights and a non-exclusive license to know-how owned or controlled by Duke to develop and commercialize any products or processes covered under the Duke License (the “Duke licensed products”). The Duke License was amended in February 2016 to allow Duke to use the Company’s technology in the area of small-molecule oncologics. The Duke License is a worldwide, sublicensable agreement and remains in full effect for the life of the last-to-expire patents included in the patent rights, which is approximately 20 years. The Company is required to apply for, prosecute and maintain all U.S. and foreign patent rights under the Duke License.

The Company is obligated to pay up to \$2.2 million upon the achievement of clinical development and regulatory milestones and up to \$0.4 million upon the achievement of commercial milestones. The Duke License may be terminated by Duke if the Company fails to meet certain clinical development and regulatory milestones within specified timeframes. As of December 31, 2018, the Company was in compliance with its development obligations.

The Company is required to use commercially reasonable efforts to develop one or more products or processes and introduce them into commercial markets. Duke will receive low single-digit royalty percentages on net sales by the Company or its sublicensee, with minimum aggregate royalties of \$0.2 million payable following the Company’s achievement of certain commercial milestones. No sales of Duke licensed products or services have occurred since the effective date through December 31, 2018.

Certain alliance fee payments up to the greater of \$0.3 million or a low double-digit percentage of the fees the Company receives from a third party in consideration of forming a strategic alliance, may be required depending upon how the patent rights are commercialized. The Company will pay Duke the first \$1.0 million of nonroyalty payments it receives from a sublicensee, and thereafter a specified percentage of any additional nonroyalty payments it receives. If Duke receives revenue as a result of a license or sublicense to a third party in the field of small-molecule oncologics, it will pay the Company a specified percentage of the amount of such revenue in excess of \$1.0 million. Duke is also a stockholder of the Company.

12. Grant Revenue

In February 2018, the Company received Small Business Innovation Research (“SBIR”) grants from the National Institutes of Health in an aggregate amount of \$2.8 million to support the clinical development of PB1046 for the treatment of pulmonary arterial hypertension for the period from February 17, 2018 to July 31, 2020. In connection with the SBIR grants, the U.S. government will receive a non-exclusive, royalty-free license to use any technology the Company develops under such grants. The Company recognized \$0.7 million under the SBIR grants in the year ended December 31, 2018. The Company did not recognize any grant revenues for the year ended December 31, 2017.

13. Income Taxes

The Company's loss before income taxes was \$23.8 million and \$10.2 million for the years ended December 31, 2018 and 2017, respectively and was generated entirely in the United States. The Company did not record current or deferred income tax expense or benefit during the years ended December 31, 2018 and 2017.

A reconciliation of income tax expense (benefit) to the amount computed by applying the statutory federal income tax rate to the loss from operations is summarized for the years ended December 31, 2018 and 2017, respectively, as follows (in thousands):

	Year Ended December 31,	
	2018	2017
Income tax benefit at statutory rate	\$ (5,008)	\$ (3,484)
State income tax, net of federal benefit	(1,593)	(528)
Permanent items	3	4
Fair value adjustments	15	(164)
Non-deductible interest expense	706	905
Stock-based compensation	45	21
Orphan drug credit	(475)	(616)
Research and development credits	(274)	(218)
Uncertain tax positions	222	209
Tax Cuts and Jobs Act	(15)	10,978
Change in valuation allowance	6,426	(7,110)
Other	(52)	3
	<u>\$ —</u>	<u>\$ —</u>

Significant components of the Company's deferred tax assets as of December 31, 2018 and 2017 are shown below:

	Year Ended December 31,	
	2018	2017
Net deferred tax asset:		
Net operating loss carryforwards	\$ 31,744	\$ 26,138
Research and development credits	4,615	3,863
Accrued expenses	332	239
Intangibles	69	110
Property and equipment	(18)	(2)
Other, net	54	22
Total net deferred tax asset	36,796	30,370
Valuation allowance for deferred tax asset	(36,796)	(30,370)
Deferred tax assets, net of valuation allowance	<u>\$ —</u>	<u>\$ —</u>

As of December 31, 2018 and 2017, management assessed the realizability of deferred tax assets and evaluated the need for a valuation allowance against the deferred tax assets. This evaluation utilizes the framework contained in ASC 740, *Income Taxes*, whereby management considers all available positive and negative evidence as of the balance sheet date to determine whether all or some portion of the Company's deferred tax assets will be realized. Under this guidance, a valuation allowance must be established for deferred tax assets when it is more-likely-than-not (a probability level of more than 50%) that the asset will not be realized.

Management followed the guidance in ASC 740, which states that “a cumulative loss in recent years is a significant piece of negative evidence that is difficult to overcome” and concluded that the Company’s deferred tax assets were not realizable as of December 31, 2018 and 2017 and recorded a valuation allowance of \$36.8 million and \$30.4 million, respectively, to offset the deferred tax assets. The change in valuation allowance for the years ended December 31, 2018 and 2017 was an increase of \$6.4 million and a decrease of \$7.1 million, respectively.

At December 31, 2018, the Company had federal and Pennsylvania net operating loss (“NOL”) carryforwards of \$111.9 million, and \$105.9 million, respectively. The federal NOLs generated prior to 2018 may be used to offset up to 100% of future taxable income and will begin to expire in 2022, unless previously utilized. The federal NOL generated in 2018 of \$20.4 million will be available to offset up to 80% of future taxable income and may be carried forward indefinitely. The Pennsylvania NOLs may be used to offset 40% of future taxable income and will begin to expire in 2029, unless previously utilized.

At December 31, 2018, the Company also has federal and Pennsylvania research and development tax credit carryforwards totaling \$3.2 million and \$0.2 million, respectively. The federal and Pennsylvania research and development tax credit carryforwards will begin to expire in 2028 and 2029, respectively, unless previously utilized.

At December 31, 2018, the Company also has federal orphan drug credit carryforwards of \$2.8 million, which will begin to expire in 2036, unless previously utilized.

For all years through December 31, 2018, the Company generated a combination of research and development credits and orphan drug credits. Certain of these credits were derived from studies to document the qualified activities and certain other credits were not derived from studies. For the credits that were calculated through a study, the IRS, on audit, may disagree with the amount of credits calculated. When studies are ultimately performed for the other credits, they may result in an adjustment to those specific credits.

Under the Internal Revenue Code, the utilization of a corporation’s net operating loss and tax credit carryforwards may be limited following a greater than 50% change in ownership over a three-year period. Any unused annual limitation may be carried forward to future years for the balance of the net operating loss and tax credit carryforward period. Under these rules, prior ownership changes may have created a limitation in the Company’s ability to use certain tax carryforwards on a yearly basis. Additionally, certain state operating losses may also be limited, including Pennsylvania, which limits net operating loss carryforward utilization to 35% (40% in 2019 and thereafter) of apportioned taxable income.

In December 2017, the U.S. government enacted comprehensive tax legislation commonly referred to as the Tax Cuts and Jobs Act (the “Tax Act”). The Tax Act makes broad and complex changes to the U.S. tax code, including, but not limited to: (i) reducing the U.S. federal corporate tax rate from 35 percent to 21 percent; (ii) eliminating the corporate alternative minimum tax (“AMT”) and changing how existing AMT credits can be realized; (iii) creating a new limitation on deductible interest expense; and (iv) changing rules related to uses and limitations of net operating carryforwards created in tax years beginning after December 31, 2017.

The Company applied the guidance in SEC Staff Accounting Bulletin 118 when accounting for the enactment-date effects of the Act in 2017 and throughout 2018. At December 31, 2017, the Company had not completed its accounting for all of the enactment-date income tax effects of the Act under ASC 740, Income Taxes, related to the remeasurement of deferred tax assets and liabilities. At December 31, 2018, the Company has now completed its accounting for all of the enactment-date income tax effects of the Act, and no adjustments were made to the provisional amounts recorded at December 31, 2017.

The most significant impact of the Tax Act on the Company's consolidated financial statements was the reduction of \$11.0 million of the deferred tax assets related to the net operating losses and other deferred tax assets. The reduction was offset by a change in the Company's valuation allowance. Another significant impact of the Tax Act was to reduce the applicable percentage to be used for the Orphan Drug Credit for tax years beginning after December 31, 2017.

The Company applies the two-step approach to recognizing and measuring uncertain tax positions. The first step is to evaluate the tax position for recognition by determining if the weight of available evidence indicates it is more likely than not that the position will be sustained on audit, including resolution of related appeals or litigation processes, if any. The second step is to measure the tax benefit as the largest amount, which is more than 50% likely of being realized upon ultimate settlement. Income tax positions must meet a more likely than not recognition threshold at the effective date to be recognized upon the adoption of ASC 740 and in subsequent periods. This interpretation also provides guidance on measurement, derecognition, classification, interest and penalties, accounting in interim periods, disclosure and transition.

The Company files income tax returns in the U.S. federal jurisdiction, and various state jurisdictions. Tax years 2015 and forward remain open for examination for federal tax purposes and tax years 2015 and forward remain open for examination for the Company's more significant state tax jurisdictions. To the extent utilized in future years' tax returns, net operating loss carryforwards at December 31, 2018 will remain subject to examination until the respective tax year is closed.

The following table summarizes the activity related to the Company's gross unrecognized tax benefits for the years ended December 31, 2018 and 2017 (in thousands):

	<u>Year Ended December 31,</u>	
	<u>2018</u>	<u>2017</u>
Gross unrecognized tax benefits at the beginning of the year	\$ 1,293	\$ 1,067
Increases related to current year positions	362	226
Increases related to prior year positions	154	—
Decreases related to prior year positions	—	—
Expiration of unrecognized tax benefits	—	—
Gross unrecognized tax benefits at the end of the year	<u>\$ 1,809</u>	<u>\$ 1,293</u>

Due to the Company's valuation allowance, none of the unrecognized tax benefits, if recognized, would affect the Company's effective tax rate.

As of December 31, 2018, and 2017, the Company had unrecognized tax benefits of \$1.8 million and \$1.3 million, respectively. The Company recognizes interest and penalties related to uncertain tax positions in income tax expense. During the years ended December 31, 2018 and 2017, the Company did not accrue any interest and penalties on uncertain tax positions. The Company does not expect its unrecognized tax benefits to change significantly within the next 12 months.

14. Related Party Transactions

As described above in Note 11, the Company is party to the MedImmune License. MedImmune is a related party of the Company.

15. Subsequent Events

On March 25, 2019, the Company entered into a term loan agreement (the “2019 Loan”) with SVB and WestRiver Innovation Lending Fund VIII, L.P. (“WestRiver”), pursuant to which the Company may borrow up to \$15.0 million, issuable in three separate tranches (“Advances”), of \$7.5 million, or Tranche A, which was issued upon execution of the SVB and WestRiver Loan Agreement, \$2.5 million available to be issued until May 31, 2019, (“Tranche B”), and \$5.0 million (“Tranche C”), which the Company will draw upon the achievement of certain regulatory milestones (the “Tranche C milestones”).

The maturity date of the 2019 Loan is March 1, 2023. Under the terms of the 2019 Loan, the Company is to make interest-only payments through December 31, 2019 on Tranche A and Tranche B at a rate equal to the greater of the Prime Rate plus 1.00%, as defined in the 2019 Loan, or 6.5%, followed by an amortization period of 39 months of equal monthly payments of principal plus interest amounts until paid in full. The interest-only period will automatically be extended to June 30, 2020 if the Company achieves the Tranche C milestones, followed by an amortization period of 33 months of equal monthly payments of principal plus interest amounts until paid in full. In addition to and not in substitution for the Company’s regular monthly payments of principal plus accrued interest, the Company is required to make a final payment equal to 6% of the aggregate principal amount of the Advances on the maturity date.

The Company has agreed to issue to SVB and WestRiver warrants to purchase shares of common stock on when we draw on each of Tranche A (an aggregate of 12,131 shares of common stock) and Tranche B (an aggregate of 24,262 shares of common stock), with an exercise price of the lower of the average closing price of the Company’s common stock for the previous ten days of trading or the closing price on the day prior to funding. The warrants are immediately exercisable upon issuance and expire ten years from the date of issuance.

Upon execution of the 2019 Loan, the Company drew \$7.5 million from Tranche A and repaid the outstanding principal balance and accrued portion of the final payment for the SVB Loan in full.

The Company’s obligations under the 2019 Loan are secured by a first priority security interest in substantially all of the Company’s current and future assets, excluding intellectual property. The Company is also obligated to comply with various other customary covenants, including restrictions on the Company’s ability to encumber its intellectual property assets.

(a)(2) Financial Statement Schedules

All financial statement schedules have been omitted as they are not required, not applicable, or the required information is included in the financial statements or notes to the financial statements.

(a)(3) Exhibits**EXHIBIT INDEX**

Exhibit Number	Exhibit Title	Incorporated by Reference			
		Form	File No.	Exhibit	Filing Date
3.1	Amended and Restated Certificate of Incorporation of PhaseBio Pharmaceuticals, Inc.	8-K	001-38697	3.1	October 22, 2018
3.2	Amended and Restated Bylaws of PhaseBio Pharmaceuticals, Inc.	S-1/A	333-227474	3.4	October 5, 2018
4.1	Form of Warrant to Purchase Shares of Series B Redeemable Convertible Preferred Stock, issued by PhaseBio Pharmaceuticals, Inc. on December 22, 2009.	S-1	333-227474	4.2	September 21, 2018
4.2	Warrant to Purchase Shares of Series C-1 Redeemable Convertible Preferred Stock, issued by PhaseBio Pharmaceuticals, Inc. to Silicon Valley Bank on October 18, 2017.	S-1	333-227474	4.3	September 21, 2018
4.3	Fourth Amended and Restated Investor Rights Agreement, by and among PhaseBio Pharmaceuticals, Inc. and certain of its stockholders, dated August 27, 2018.	S-1	333-227474	4.4	September 21, 2018
4.4#	Warrant to Purchase Shares of Common Stock, issued by PhaseBio Pharmaceuticals, Inc. to Silicon Valley Bank on March 25, 2019.				
4.5#	Warrant to Purchase Shares of Common Stock, issued by PhaseBio Pharmaceuticals, Inc. to WestRiver Innovation Lending Fund VIII, L.P. on March 25, 2019.				
10.1+	2018 Equity Incentive Plan and Forms of Stock Option Grant Notice and Agreement and Restricted Stock Unit Grant Notice and Agreement thereunder.	S-8	333-227935	10.2	October 22, 2018
10.2+	2018 Employee Stock Purchase Plan.	S-8	333-227935	10.3	October 22, 2018
10.3+	Non-Employee Director Compensation Policy.	S-1/A	333-227474	10.4	October 5, 2018

Exhibit Number	Exhibit Title	Incorporated by Reference			
		Form	File No.	Exhibit	Filing Date
10.4+	Form of Indemnification Agreement by and between PhaseBio Pharmaceuticals, Inc. and each of its directors and executive officers.	S-1/A	333-227474	10.5	October 5, 2018
10.5+	Severance Benefit Plan and Form of Participation Agreement.	S-1/A	333-227474	10.6.1	October 5, 2018
10.6+	Amended and Restated 2002 Stock Plan and Form of Option Agreement and Exercise Notice thereunder, as amended to date.	S-1	333-227474	10.1	September 21, 2018
10.7+	Offer Letter, dated as of November 19, 2012, by and between PhaseBio Pharmaceuticals, Inc. and Jonathan P. Mow, as amended to date.	S-1	333-227474	10.7	September 21, 2018
10.8+	Offer Letter, dated as of March 13, 2016, by and between PhaseBio Pharmaceuticals, Inc. and John Sharp.	S-1	333-227474	10.8	September 21, 2018
10.9+	Offer Letter, dated as of November 19, 2012, by and between PhaseBio Pharmaceuticals, Inc. and John Lee, M.D., Ph.D.	S-1	333-227474	10.9	September 21, 2018
10.10†	License Agreement, dated as of October 18, 2017 and as amended to date, by and between Phase Bioscience, Inc. (predecessor to PhaseBio Pharmaceuticals, Inc.) and Duke University	S-1	333-227474	10.10	September 21, 2018
10.11†	License Agreement, dated as of November 21, 2017, by and between PhaseBio Pharmaceuticals, Inc. and MedImmune Limited.	S-1	333-227474	10.11	September 21, 2018
10.12	Loan and Security Agreement, dated as of October 18, 2017 and as amended to date, by and between PhaseBio Pharmaceuticals, Inc. and Silicon Valley Bank.	S-1	333-227474	10.12	September 21, 2018
10.13#	Loan and Security Agreement, dated as of March 25, 2019, by and among PhaseBio Pharmaceuticals, Inc. and Silicon Valley Bank and WestRiver Innovation Lending Fund VIII, L.P.				
10.14#††	Master Services Agreement, dated as of November 14, 2018, by and between PhaseBio Pharmaceuticals, Inc. and BioVectra Inc.				

Exhibit Number	Exhibit Title	Incorporated by Reference			
		Form	File No.	Exhibit	Filing Date
10.15	Lease Agreement, dated as of January 15, 2010 and as amended to date, by and between PhaseBio Pharmaceuticals, Inc. and Liberty Property Limited Partnership.	S-1	333-227474	10.13	September 21, 2018
23.1#	Consent of KPMG LLP				
24.1#	Power of Attorney				
31.1#	Certification of Chief Executive Officer and President (Principal Executive Officer), pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				
31.2#	Certification of Chief Financial Officer (Principal Financial Officer), pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				
32.1##*	Certification of Chief Executive Officer (Principal Executive Officer), pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				
32.2##*	Certification of Chief Financial Officer (Principal Financial Officer), pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				
101.INS#	XBRL Instance Document.				
101.SCH#	XBRL Taxonomy Extension Schema Document.				
101.CAL#	XBRL Taxonomy Extension Calculation Linkbase Document.				
101.DEF#	XBRL Taxonomy Extension Definition Linkbase Document.				
101.LAB#	XBRL Taxonomy Extension Label Linkbase Document.				
101.PRE#	XBRL Taxonomy Extension Presentation Linkbase Document.				
#	Filed herewith.				
+	Indicates management contract or compensatory plan.				
†	Confidential treatment has been granted for certain portions of this exhibit (indicated by asterisks). Such information has been omitted and was filed separately with the Securities and Exchange Commission.				
††	Certain portions of this exhibit (indicated by asterisks) have been omitted because they are not material and would likely cause competitive harm to PhaseBio Pharmaceuticals, Inc. if publicly disclosed.				

* These certifications are being furnished solely to accompany this quarterly report pursuant to 18 U.S.C. Section 1350, and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and are not to be incorporated by reference into any filing of the registrant, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

Item 16. Form 10-K Summary

Not applicable.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

PHASEBIO PHARMACEUTICALS INC.

March 26, 2019

By: /s/ John Sharp
 John Sharp
 Chief Financial Officer
*(On behalf of the registrant and in his capacity as
 Principal Financial Officer and Principal Accounting Officer)*

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Jonathan P. Mow and John Sharp, jointly and severally, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign this Annual Report on Form 10-K of PhaseBio Pharmaceuticals, Inc., and any or all amendments thereto, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises hereby ratifying and confirming all that said attorneys-in-fact and agents, or his, her or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof. Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
<u>/s/ Jonathan P. Mow</u> Jonathan P. Mow	Chief Executive Officer and Director <i>(Principal Executive Officer)</i>	March 26, 2019
<u>/s/ John Sharp</u> John Sharp	Chief Financial Officer <i>(Principal Financial Officer and Principal Accounting Officer)</i>	March 26, 2019
<u>/s/ Clay B. Thorp</u> Clay B. Thorp	Chairman of the Board of Directors	March 26, 2019
<u>/s/ Edmund P. Harrigan, M.D.</u> Edmund P. Harrigan, M.D.	Director	March 26, 2019
<u>/s/ Nancy J. Hutson, Ph.D.</u> Nancy J. Hutson, Ph.D.	Director	March 26, 2019
<u>/s/ Peter Justin Klein, M.D., J.D.</u> Peter Justin Klein, M.D., J.D.	Director	March 26, 2019
<u>/s/ Caroline Loewy</u> Caroline Loewy	Director	March 26, 2019
<u>/s/ Bibhash Mukhopadhyay, Ph.D.</u> Bibhash Mukhopadhyay, Ph.D.	Director	March 26, 2019
<u>/s/ Linda Tufts</u> Linda Tufts	Director	March 26, 2019
<u>/s/ Richard A. van den Broek</u> Richard A. van den Broek	Director	March 26, 2019

THIS WARRANT AND THE SHARES ISSUABLE HEREUNDER HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "ACT"), OR THE SECURITIES LAWS OF ANY STATE AND, EXCEPT AS SET FORTH IN SECTIONS 5.3 AND 5.4 BELOW, MAY NOT BE OFFERED, SOLD, PLEDGED OR OTHERWISE TRANSFERRED UNLESS AND UNTIL REGISTERED UNDER SAID ACT AND LAWS OR IN FORM AND SUBSTANCE SATISFACTORY TO THE COMPANY, SUCH OFFER, SALE, PLEDGE OR OTHER TRANSFER IS EXEMPT FROM SUCH REGISTRATION.

WARRANT TO PURCHASE COMMON STOCK

Company: PHASEBIO PHARMACEUTICALS, INC.

Number of Shares of Common Stock: 18,803

Warrant Price: \$4.73 per share

Issue Date: March 25, 2019

Expiration Date: March 25, 2029 **See also Section 5.1(b).**

Credit Facility: This Warrant to Purchase Common Stock ("**Warrant**") is issued in connection with that certain Loan and Security Agreement dated as of March 25, 2019 by and among Silicon Valley Bank, WestRiver Innovation Lending Fund VIII, L.P. and the Company (as the same may from time to time be amended, modified, supplemented or restated) (the "**Loan Agreement**").

THIS WARRANT CERTIFIES THAT, for good and valuable consideration, SILICON VALLEY BANK (together with any successor or permitted assignee or transferee of this Warrant or of any shares issued upon exercise hereof, "**Holder**") is entitled to purchase the number of fully paid and non-assessable shares (the "**Shares**") of the above-stated common stock (the "**Common Stock**") of the above-named company (the "**Company**") at the above-stated Warrant Price, all as set forth above and as adjusted pursuant to Section 2 of this Warrant, subject to the provisions and upon the terms and conditions set forth in this Warrant. Reference is made to Section 5.4 of this Warrant whereby Silicon Valley Bank shall transfer this Warrant to its parent company, SVB Financial Group.

SECTION 1. EXERCISE.

1.1 Method of Exercise. Holder may at any time and from time to time through 6:00 PM, Pacific time, on the Expiration Date, exercise this Warrant, in whole or in part, by delivering to the Company the original of this Warrant together with a duly executed Notice of Exercise in substantially the form attached hereto as Appendix 1 and, unless Holder is exercising this Warrant pursuant to a cashless exercise set forth in Section 1.2, a check, wire transfer of same-day funds (to an account designated by the Company), or other form of payment acceptable to the Company for the aggregate Warrant Price for the Shares being purchased.

1.2 Cashless Exercise. On any exercise of this Warrant, in lieu of payment of the aggregate Warrant Price in the manner as specified in Section 1.1 above, but otherwise in accordance with the requirements of Section 1.1, Holder may elect to receive Shares equal to the value of this Warrant, or portion hereof as to which this Warrant is being exercised. Thereupon, the Company shall issue to the Holder such number of fully paid and non-assessable Shares as are computed using the following formula:

$$X = Y(A-B)/A$$

where:

- X = the number of Shares to be issued to the Holder;
- Y = the number of Shares with respect to which this Warrant is being exercised (inclusive of the Shares surrendered to the Company in payment of the aggregate Warrant Price);
- A = the Fair Market Value (as determined pursuant to Section 1.3 below) of one Share; and
- B = the Warrant Price.

1.3 Fair Market Value. If the Company's Common Stock is then traded or quoted on a nationally recognized securities exchange, inter-dealer quotation system or over-the-counter market (a "**Trading Market**"), the fair market value of a Share shall be the closing price or last sale price of a share of Common Stock reported for the Business Day immediately before the date on which Holder delivers this Warrant together with its Notice of Exercise to the Company. If the Company's Common Stock is not traded in a Trading Market, the Board of Directors of the Company shall determine the fair market value of a Share in its reasonable good faith judgment.

1.4 Delivery of Certificate and New Warrant. Within a reasonable time after Holder exercises this Warrant in the manner set forth in Section 1.1 or 1.2 above, the Company shall deliver to Holder a certificate representing the Shares issued to Holder upon such exercise (which certificate may be in the form of an electronic certificate or DTC entry, to the extent used by the Company at the time of such exercise) and, if this Warrant has not been fully exercised and has not expired, a new warrant of like tenor representing the Shares not so acquired.

1.5 Replacement of Warrant. On receipt of evidence reasonably satisfactory to the Company of the loss, theft, destruction or mutilation of this Warrant and, in the case of loss, theft or destruction, on delivery of an indemnity agreement reasonably satisfactory in form, substance and amount to the Company or, in the case of mutilation, on surrender of this Warrant to the Company for cancellation, the Company shall, within a reasonable time, execute and deliver to Holder, in lieu of this Warrant, a new warrant of like tenor and amount.

1.6 Treatment of Warrant Upon Acquisition of Company.

(a) Acquisition. For the purpose of this Warrant, "**Acquisition**" means any transaction or series of related transactions involving: (i) the sale, lease, exclusive license, or other disposition of all or substantially all of the assets of the Company (ii) any merger or consolidation of the Company into or with another person or entity (other than a merger or consolidation effected exclusively to change the Company's domicile), or any other corporate reorganization, in which the stockholders of the Company in their capacity as such immediately prior to such merger, consolidation or reorganization, own less than a majority of the Company's (or the surviving or successor entity's) outstanding voting power immediately after such merger, consolidation or reorganization; or (iii) any sale or other transfer by the stockholders of the Company of shares representing at least a majority of the Company's then-total outstanding combined voting power.

(b) Treatment of Warrant at Acquisition. In the event of an Acquisition in which the consideration to be received by the Company's stockholders consists solely of cash, solely of Marketable Securities or a combination of cash and Marketable Securities (a "**Cash/Public Acquisition**"), and the fair market value of one Share as determined in accordance with Section 1.3 above would be greater than the Warrant Price in effect on such date immediately prior to such Cash/Public Acquisition, and Holder has not exercised this Warrant pursuant to Section 1.1 above as to all Shares, then this Warrant shall automatically be deemed to be Cashless Exercised pursuant to Section 1.2 above as to all Shares effective immediately prior to and contingent upon the consummation of a Cash/Public Acquisition. In connection with such Cashless Exercise, Holder shall be deemed to have restated each of the representations and warranties in Section 4 of the Warrant as the date thereof and the Company shall promptly notify the Holder of the number of Shares (or such other securities) issued upon exercise. In the event of a Cash/Public Acquisition where the fair market value of one Share as determined in accordance with Section 1.3 above would be less than the Warrant Price in effect immediately prior to such Cash/Public Acquisition, then this Warrant will expire immediately prior to the consummation of such Cash/Public Acquisition.

(c) Upon the closing of any Acquisition other than a Cash/Public Acquisition, the acquiring, surviving or successor entity shall assume the obligations of this Warrant, and this Warrant shall thereafter be exercisable for the same securities and/or other property as would have been paid for the Shares issuable upon exercise of the unexercised portion of this Warrant as if such Shares were outstanding on and as of the closing of such Acquisition, subject to further adjustment from time to time in accordance with the provisions of this Warrant.

(d) As used in this Warrant, "**Marketable Securities**" means securities meeting all of the following requirements: (i) the issuer thereof is then subject to the reporting requirements of Section 13 or Section 15(d) of the Securities Exchange Act of 1934, as amended (the "**Exchange Act**"), and is then current in its filing of all required reports and other information under the Act and the Exchange Act; (ii) the class and series of shares or other security of the issuer that would be received by Holder in connection with the Acquisition were Holder to exercise this Warrant on or prior to the closing thereof is then traded in a Trading Market, and (iii) following the closing of such Acquisition, Holder would not be restricted from publicly reselling all of the issuer's shares and/or other securities that would be received by Holder in such Acquisition were Holder to exercise or convert this Warrant in full on or prior to the closing of such Acquisition, except to the extent that any such restriction (x) arises solely under federal or state securities laws, rules or regulations, and (y) does not extend beyond six (6) months from the closing of such Acquisition.

SECTION 2. ADJUSTMENTS TO THE SHARES AND WARRANT PRICE.

2.1 Stock Dividends, Splits, Etc. If the Company declares or pays a dividend or distribution on the outstanding shares of the Common Stock payable in securities or property (other than cash), then upon exercise of this Warrant, for each Share acquired, Holder shall receive, without additional cost to Holder, the total number and kind of securities and property which Holder would have received had Holder owned the Shares of record as of the date the dividend or distribution occurred. If the Company subdivides the outstanding shares of the Common Stock by reclassification or otherwise into a greater number of shares, the number of Shares purchasable hereunder shall be proportionately increased and the Warrant Price shall be proportionately decreased. If the outstanding shares of the Common Stock are combined or consolidated, by reclassification or otherwise, into a lesser number of shares, the Warrant Price shall be proportionately increased and the number of Shares shall be proportionately decreased.

2.2 Reclassification, Exchange, Combinations or Substitution. Upon any event whereby all of the outstanding shares of the Common Stock are reclassified, exchanged, combined, substituted, or replaced for, into, with or by Company securities of a different class and/or series, then from and after the consummation of such event, this Warrant will be exercisable for the number, class and series of Company securities that Holder would have received had the Shares been outstanding on and as of the consummation of such event, and subject to further adjustment thereafter from time to time in accordance with the provisions of this Warrant. The provisions of this Section 2.2 shall similarly apply to successive reclassifications, exchanges, combinations substitutions, replacements or other similar events.

2.3 Intentionally Omitted.

2.4 Intentionally Omitted.

2.5 No Fractional Share. No fractional Share shall be issuable upon exercise of this Warrant and the number of Shares to be issued shall be rounded down to the nearest whole Share. If a fractional Share interest arises upon any exercise of the Warrant, the Company shall eliminate such fractional Share interest by paying Holder in cash the amount computed by multiplying the fractional interest by (i) the fair market value (as determined in accordance with Section 1.3 above) of a full Share, less (ii) the then-effective Warrant Price.

2.6 Notice/Certificate as to Adjustments. Upon each adjustment of the Warrant Price, Common Stock and/or number of Shares, the Company, at the Company's expense, shall notify Holder in writing within a reasonable time setting forth the adjustments to the Warrant Price, class and/or number of Shares and facts upon which such adjustment is based. The Company shall, upon written request from Holder, furnish Holder with a certificate of its Chief Financial Officer, including computations of such adjustment and the Warrant Price, class and number of Shares in effect upon the date of such adjustment.

SECTION 3. REPRESENTATIONS AND COVENANTS OF THE COMPANY.

3.1 Representations and Warranties. The Company represents and warrants to, and agrees with, the Holder that all Shares which may be issued upon the exercise of this Warrant, shall, upon issuance, be duly authorized, validly issued, fully paid and non-assessable, and free of any liens and encumbrances except for restrictions on transfer provided for herein or under applicable federal and state securities laws. The Company covenants that it shall at all times cause to be reserved and kept available out of its authorized and unissued capital stock such number of securities as will be sufficient to permit the exercise in full of this Warrant.

3.2 Notice of Certain Events. If the Company proposes at any time to:

(a) declare any dividend or distribution upon the outstanding shares of the Company's stock, whether in cash, property, stock, or other securities and whether or not a regular cash dividend;

(b) offer for subscription or sale pro rata to the holders of the outstanding shares any additional shares of any class or series of the Company's stock (other than pursuant to contractual pre-emptive rights);

(c) effect any reclassification, exchange, combination, substitution, reorganization or recapitalization of the outstanding shares of the Common Stock; or

(d) effect an Acquisition or to liquidate, dissolve or wind up; then, in connection with each such event, the Company shall give Holder notice thereof at the same time and in the same manner as given to holders of the outstanding shares of the Common Stock.

SECTION 4. REPRESENTATIONS, WARRANTIES OF THE HOLDER.

The Holder represents and warrants to the Company as follows:

4.1 Purchase for Own Account. This Warrant and the Shares to be acquired upon exercise of this Warrant by Holder are being acquired for investment for Holder's account, not as a nominee or agent, and not with a view to the public resale or distribution within the meaning of the Act. Holder also represents that it has not been formed for the specific purpose of acquiring this Warrant or the Shares.

4.2 Disclosure of Information. Holder is aware of the Company's business affairs and financial condition and has received or has had full access to all the information it considers necessary or appropriate to make an informed investment decision with respect to the acquisition of this Warrant and its underlying securities. Holder further has had an opportunity to ask questions and receive answers from the Company regarding the terms and conditions of the offering of this Warrant and its underlying securities and to obtain additional information (to the extent the Company possessed such information or could acquire it without unreasonable effort or expense) necessary to verify any information furnished to Holder or to which Holder has access.

4.3 Investment Experience. Holder understands that the purchase of this Warrant and its underlying securities involves substantial risk. Holder has experience as an investor in securities of companies in the development stage and acknowledges that Holder can bear the economic risk of such Holder's investment in this Warrant and its underlying securities and has such knowledge and experience in financial or business matters that Holder is capable of evaluating the merits and risks of its investment in this Warrant and its underlying securities and/or has a preexisting personal or business relationship with the Company and certain of its officers, directors or controlling persons of a nature and duration that enables Holder to be aware of the character, business acumen and financial circumstances of such persons.

4.4 Accredited Investor Status. Holder is an "accredited investor" within the meaning of Regulation D promulgated under the Act.

4.5 The Act. Holder understands that this Warrant and the Shares issuable upon exercise hereof have not been registered under the Act in reliance upon a specific exemption therefrom, which exemption depends upon, among other things, the bona fide nature of the Holder's investment intent and the accuracy of the Holder's representations and warranties as expressed herein. Holder understands that this Warrant and the Shares issued upon any exercise hereof must be held indefinitely unless subsequently registered under the Act and qualified under applicable state securities laws, or unless exemption from such registration and qualification are otherwise available. Holder is aware of the provisions of Rule 144 promulgated under the Act.

4.6 No Shareholder Rights. Without limiting any provision of this Warrant, Holder agrees that as a Holder of this Warrant it will not have any rights (including, but not limited to, voting rights) as a shareholder of the Company with respect to the Shares issuable hereunder unless and until the exercise of this Warrant and then only with respect to the Shares issued on such exercise.

SECTION 5. MISCELLANEOUS.

5.1 Term and Automatic Cashless Exercise Upon Expiration.

(a) Term. Subject to the provisions of Section 1.6 above, this Warrant is exercisable in whole or in part at any time and from time to time on or before 6:00 PM, Pacific time, on the Expiration Date and shall be void thereafter.

(b) Automatic Cashless Exercise upon Expiration. In the event that, upon the Expiration Date, the fair market value of one Share (or other security issuable upon the exercise hereof) as determined in accordance with Section 1.3 above is greater than the Warrant Price in effect on such date, then this Warrant shall automatically be deemed on and as of such date to be exercised pursuant to Section 1.2 above as to all Shares (or such other securities) for which it shall not previously have been exercised, and the Company shall, within a reasonable time, cause its transfer agent and registrar to register in book-entry form, or to deliver to the Holder a certificate representing, the Shares (or such other securities) issued upon such exercise to Holder (which certificate may be in the form of an electronic certificate or DTC entry, to the extent used by the Company at the time of such exercise).

5.2 Legends. The Shares shall be imprinted with a legend in substantially the following form:

THE SHARES EVIDENCED BY THIS CERTIFICATE HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE “**ACT**”), OR THE SECURITIES LAWS OF ANY STATE AND, EXCEPT AS SET FORTH IN THAT CERTAIN WARRANT TO PURCHASE COMMON STOCK ISSUED BY THE ISSUER TO SILICON VALLEY BANK DATED MARCH 25, 2019, MAY NOT BE OFFERED, SOLD, PLEDGED OR OTHERWISE TRANSFERRED UNLESS AND UNTIL REGISTERED UNDER SAID ACT AND LAWS OR, IN THE OPINION OF LEGAL COUNSEL IN FORM AND SUBSTANCE SATISFACTORY TO THE ISSUER, SUCH OFFER, SALE, PLEDGE OR OTHER TRANSFER IS EXEMPT FROM SUCH REGISTRATION.

5.3 Compliance with Securities Laws on Transfer. This Warrant and the Shares issuable upon exercise of this Warrant may not be transferred or assigned in whole or in part except in compliance with applicable federal and state securities laws by the transferor and the transferee (including, without limitation, the delivery of investment representation letters and legal opinions reasonably satisfactory to the Company, as reasonably requested by the Company). The Company shall not require Holder to provide an opinion of counsel if the transfer is to SVB Financial Group (Silicon Valley Bank’s parent company) or any other affiliate of Holder, provided that any such transferee is an “accredited investor” as defined in Regulation D promulgated under the Act. Additionally, the Company shall also not require an opinion of counsel if there is no material question as to the availability of Rule 144 promulgated under the Act.

5.4 Transfer Procedure. After receipt by Silicon Valley Bank of the executed Warrant, Silicon Valley Bank will transfer all of this Warrant to its parent company, SVB Financial Group. By its acceptance of this Warrant, SVB Financial Group hereby makes to the Company each of the representations and warranties set forth in Section 4 hereof and agrees to be bound by all of the terms and conditions of this Warrant as if the original Holder hereof. Subject to the provisions of Section 5.3 and upon providing the Company with written notice, SVB Financial Group and any subsequent Holder may transfer all or part of this Warrant or the Shares issuable upon exercise of this Warrant to any transferee, provided, however, in

connection with any such transfer, SVB Financial Group or any subsequent Holder will give the Company notice of the portion of the Warrant being transferred with the name, address and taxpayer identification number of the transferee and Holder will surrender this Warrant to the Company for reissuance to the transferee(s) (and Holder if applicable); and provided further, that any subsequent transferee other than SVB Financial Group shall agree in writing with the Company to be bound by all of the terms and conditions of this Warrant.

Notwithstanding anything to the contrary contained herein, so long as no Event of Default has occurred and is continuing, the Holder shall not transfer any portion of this Warrant to a direct competitor of the Company or a vulture fund, in each case as reasonably determined by the Holder, without the Company's consent, other than in connection with (x) assignments by the Holder due to a forced divestiture at the request of any regulatory agency, or (y) upon the occurrence of a default, event of default or similar occurrence with respect to the Holder's own financing or securitization transactions.

5.5 Notices. All notices and other communications hereunder from the Company to the Holder, or vice versa, shall be deemed delivered and effective (i) when given personally, (ii) on the third (3rd) Business Day after being mailed by first-class registered or certified mail, postage prepaid, (iii) upon actual receipt if given by facsimile or electronic mail and such receipt is confirmed in writing by the recipient, or (iv) on the first Business Day following delivery to a reliable overnight courier service, courier fee prepaid, in any case at such address as may have been furnished to the Company or Holder, as the case may be, in writing by the Company or such Holder from time to time in accordance with the provisions of this Section 5.5. All notices to Holder shall be addressed as follows until the Company receives notice of a change of address in connection with a transfer or otherwise:

SVB Financial Group
Attn: Treasury Department
3003 Tasman Drive, HC 215
Santa Clara, CA 95054
Telephone: (408) 654-7400
Facsimile: (408) 988-8317
Email address: derivatives@svb.com

Notice to the Company shall be addressed as follows until Holder receives notice of a change in address:

PHASEBIO PHARMACEUTICALS, INC.
1 Great Valley Parkway, Suite 30
Malvern, PA 19355
Attn: Jonathan Mow, CEO
Email: jonathan.mow@phasebio.com

With a copy (which shall not constitute notice) to:

COOLEY LLP
Attn: Christian Plaza
11951 Freedom Drive, 14th Floor
Reston, VA 20190
Telephone: (703) 456-8006
Fax: (703) 456-8100
Email: cplaza@cooley.com

5.6 Waiver. This Warrant and any term hereof may be changed, waived, discharged or terminated (either generally or in a particular instance and either retroactively or prospectively) only by an instrument in writing signed by the party against which enforcement of such change, waiver, discharge or termination is sought.

5.7 Attorney's Fees. In the event of any dispute between the parties concerning the terms and provisions of this Warrant, the party prevailing in such dispute shall be entitled to collect from the other party all costs incurred in such dispute, including reasonable attorneys' fees.

5.8 Counterparts; Facsimile/Electronic Signatures. This Warrant may be executed in counterparts, all of which together shall constitute one and the same agreement. Any signature page delivered electronically or by facsimile shall be binding to the same extent as an original signature page with regards to any agreement subject to the terms hereof or any amendment thereto.

5.9 Governing Law. This Warrant shall be governed by and construed in accordance with the laws of the State of California, without giving effect to its principles regarding conflicts of law.

5.10 Headings. The headings in this Warrant are for purposes of reference only and shall not limit or otherwise affect the meaning of any provision of this Warrant.

5.11 Business Days. "**Business Day**" is any day that is not a Saturday, Sunday or a day on which Silicon Valley Bank is closed.

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IN WITNESS WHEREOF, the parties have caused this Warrant to Purchase Common Stock to be executed by their duly authorized representatives effective as of the Issue Date written above.

“COMPANY”

PHASEBIO PHARMACEUTICALS, INC.

By: /s/ Jonathan P. Mow

Name: Jonathan P. Mow

Title: CEO

“HOLDER”

SILICON VALLEY BANK

By: /s/ Myron O. Jensen

Name: Myron O. Jensen

Title: Vice President

[Signature Page to Warrant to Purchase Common Stock]

APPENDIX 1

NOTICE OF EXERCISE

1. The undersigned Holder hereby exercises its right to purchase _____ shares of the Common Stock of **PHASEBIO PHARMACEUTICALS, INC.** (the "**Company**") in accordance with the attached Warrant To Purchase Common Stock, and tenders payment of the aggregate Warrant Price for such shares as follows:

- check in the amount of \$_____ payable to order of the Company enclosed herewith
- Wire transfer of immediately available funds to the Company's account
- Cashless Exercise pursuant to Section 1.2 of the Warrant
- Other [Describe] _____

2. Please issue a certificate or certificates representing the Shares in the name specified below:

Holder's Name

(Address)

3. By its execution below and for the benefit of the Company, Holder hereby restates each of the representations and warranties in Section 4 of the Warrant to Purchase Common Stock as of the date hereof.

HOLDER:

By: _____
Name: _____
Title: _____
(Date): _____

THIS WARRANT AND THE SHARES ISSUABLE HEREUNDER HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "ACT"), OR THE SECURITIES LAWS OF ANY STATE AND, EXCEPT AS SET FORTH IN SECTIONS 5.3 AND 5.4 BELOW, MAY NOT BE OFFERED, SOLD, PLEDGED OR OTHERWISE TRANSFERRED UNLESS AND UNTIL REGISTERED UNDER SAID ACT AND LAWS OR IN FORM AND SUBSTANCE SATISFACTORY TO THE COMPANY, SUCH OFFER, SALE, PLEDGE OR OTHER TRANSFER IS EXEMPT FROM SUCH REGISTRATION.

WARRANT TO PURCHASE COMMON STOCK

Company: PHASEBIO PHARMACEUTICALS, INC.

Number of Shares of Common Stock: 18,803

Warrant Price: \$4.73 per share

Issue Date: March 25, 2019

Expiration Date: March 25, 2029 **See also Section 5.1(b).**

Credit Facility: This Warrant to Purchase Common Stock ("**Warrant**") is issued in connection with that certain Loan and Security Agreement dated as of March 25, 2019 by and among Silicon Valley Bank, WestRiver Innovation Lending Fund VIII, L.P. and the Company (as the same may from time to time be amended, modified, supplemented or restated) (the "**Loan Agreement**").

THIS WARRANT CERTIFIES THAT, for good and valuable consideration, WESTRIVER INNOVATION LENDING FUND VIII, L.P. (together with any successor or permitted assignee or transferee of this Warrant or of any shares issued upon exercise hereof, "**Holder**") is entitled to purchase the number of fully paid and non-assessable shares (the "**Shares**") of the above-stated common stock (the "**Common Stock**") of the above-named company (the "**Company**") at the above-stated Warrant Price, all as set forth above and as adjusted pursuant to Section 2 of this Warrant, subject to the provisions and upon the terms and conditions set forth in this Warrant.

SECTION 1. EXERCISE.

1.1 Method of Exercise. Holder may at any time and from time to time through 6:00 PM, Pacific time, on the Expiration Date, exercise this Warrant, in whole or in part, by delivering to the Company the original of this Warrant together with a duly executed Notice of Exercise in substantially the form attached hereto as Appendix 1 and, unless Holder is exercising this Warrant pursuant to a cashless exercise set forth in Section 1.2, a check, wire transfer of same-day funds (to an account designated by the Company), or other form of payment acceptable to the Company for the aggregate Warrant Price for the Shares being purchased.

1.2 Cashless Exercise. On any exercise of this Warrant, in lieu of payment of the aggregate Warrant Price in the manner as specified in Section 1.1 above, but otherwise in accordance with the requirements of Section 1.1, Holder may elect to receive Shares equal to the value of this Warrant, or portion hereof as to which this Warrant is being exercised. Thereupon, the Company shall issue to the Holder such number of fully paid and non-assessable Shares as are computed using the following formula:

$$X = Y(A-B)/A$$

where:

- X = the number of Shares to be issued to the Holder;
- Y = the number of Shares with respect to which this Warrant is being exercised (inclusive of the Shares surrendered to the Company in payment of the aggregate Warrant Price);
- A = the Fair Market Value (as determined pursuant to Section 1.3 below) of one Share; and
- B = the Warrant Price.

1.3 Fair Market Value. If the Company's Common Stock is then traded or quoted on a nationally recognized securities exchange, inter-dealer quotation system or over-the-counter market (a "**Trading Market**"), the fair market value of a Share shall be the closing price or last sale price of a share of Common Stock reported for the Business Day immediately before the date on which Holder delivers this Warrant together with its Notice of Exercise to the Company. If the Company's Common Stock is not traded in a Trading Market, the Board of Directors of the Company shall determine the fair market value of a Share in its reasonable good faith judgment.

1.4 Delivery of Certificate and New Warrant. Within a reasonable time after Holder exercises this Warrant in the manner set forth in Section 1.1 or 1.2 above, the Company shall deliver to Holder a certificate representing the Shares issued to Holder upon such exercise (which certificate may be in the form of an electronic certificate or DTC entry, to the extent used by the Company at the time of such exercise) and, if this Warrant has not been fully exercised and has not expired, a new warrant of like tenor representing the Shares not so acquired.

1.5 Replacement of Warrant. On receipt of evidence reasonably satisfactory to the Company of the loss, theft, destruction or mutilation of this Warrant and, in the case of loss, theft or destruction, on delivery of an indemnity agreement reasonably satisfactory in form, substance and amount to the Company or, in the case of mutilation, on surrender of this Warrant to the Company for cancellation, the Company shall, within a reasonable time, execute and deliver to Holder, in lieu of this Warrant, a new warrant of like tenor and amount.

1.6 Treatment of Warrant Upon Acquisition of Company.

(a) Acquisition. For the purpose of this Warrant, "**Acquisition**" means any transaction or series of related transactions involving: (i) the sale, lease, exclusive license, or other disposition of all or substantially all of the assets of the Company (ii) any merger or consolidation of the Company into or with another person or entity (other than a merger or consolidation effected exclusively to change the Company's domicile), or any other corporate reorganization, in which the stockholders of the Company in their capacity as such immediately prior to such merger, consolidation or reorganization, own less than a majority of the Company's (or the surviving or successor entity's) outstanding voting power immediately after such merger, consolidation or reorganization; or (iii) any sale or other transfer by the stockholders of the Company of shares representing at least a majority of the Company's then-total outstanding combined voting power.

(b) Treatment of Warrant at Acquisition. In the event of an Acquisition in which the consideration to be received by the Company's stockholders consists solely of cash, solely of Marketable Securities or a combination of cash and Marketable Securities (a "**Cash/Public Acquisition**"), and the fair market value of one Share as determined in accordance with Section 1.3 above would be greater than the Warrant Price in effect on such date immediately prior to such Cash/Public Acquisition, and Holder has not exercised this Warrant pursuant to Section 1.1 above as to all Shares, then this Warrant shall automatically be deemed to be Cashless Exercised pursuant to Section 1.2 above as to all Shares effective immediately prior to and contingent upon the consummation of a Cash/Public Acquisition. In connection with such Cashless Exercise, Holder shall be deemed to have restated each of the representations and warranties in Section 4 of the Warrant as the date thereof and the Company shall promptly notify the Holder of the number of Shares (or such other securities) issued upon exercise. In the event of a Cash/Public Acquisition where the fair market value of one Share as determined in accordance with Section 1.3 above would be less than the Warrant Price in effect immediately prior to such Cash/Public Acquisition, then this Warrant will expire immediately prior to the consummation of such Cash/Public Acquisition.

(c) Upon the closing of any Acquisition other than a Cash/Public Acquisition, the acquiring, surviving or successor entity shall assume the obligations of this Warrant, and this Warrant shall thereafter be exercisable for the same securities and/or other property as would have been paid for the Shares issuable upon exercise of the unexercised portion of this Warrant as if such Shares were outstanding on and as of the closing of such Acquisition, subject to further adjustment from time to time in accordance with the provisions of this Warrant.

(d) As used in this Warrant, "**Marketable Securities**" means securities meeting all of the following requirements: (i) the issuer thereof is then subject to the reporting requirements of Section 13 or Section 15(d) of the Securities Exchange Act of 1934, as amended (the "**Exchange Act**"), and is then current in its filing of all required reports and other information under the Act and the Exchange Act; (ii) the class and series of shares or other security of the issuer that would be received by Holder in connection with the Acquisition were Holder to exercise this Warrant on or prior to the closing thereof is then traded in a Trading Market, and (iii) following the closing of such Acquisition, Holder would not be restricted from publicly reselling all of the issuer's shares and/or other securities that would be received by Holder in such Acquisition were Holder to exercise or convert this Warrant in full on or prior to the closing of such Acquisition, except to the extent that any such restriction (x) arises solely under federal or state securities laws, rules or regulations, and (y) does not extend beyond six (6) months from the closing of such Acquisition.

SECTION 2. ADJUSTMENTS TO THE SHARES AND WARRANT PRICE.

2.1 Stock Dividends, Splits, Etc. If the Company declares or pays a dividend or distribution on the outstanding shares of the Common Stock payable in securities or property (other than cash), then upon exercise of this Warrant, for each Share acquired, Holder shall receive, without additional cost to Holder, the total number and kind of securities and property which Holder would have received had Holder owned the Shares of record as of the date the dividend or distribution occurred. If the Company subdivides the outstanding shares of the Common Stock by reclassification or otherwise into a greater number of shares, the number of Shares purchasable hereunder shall be proportionately increased and the Warrant Price shall be proportionately decreased. If the outstanding shares of the Common Stock are combined or consolidated, by reclassification or otherwise, into a lesser number of shares, the Warrant Price shall be proportionately increased and the number of Shares shall be proportionately decreased.

2.2 Reclassification, Exchange, Combinations or Substitution. Upon any event whereby all of the outstanding shares of the Common Stock are reclassified, exchanged, combined, substituted, or replaced for, into, with or by Company securities of a different class and/or series, then from and after the consummation of such event, this Warrant will be exercisable for the number, class and series of Company securities that Holder would have received had the Shares been outstanding on and as of the consummation of such event, and subject to further adjustment thereafter from time to time in accordance with the provisions of this Warrant. The provisions of this Section 2.2 shall similarly apply to successive reclassifications, exchanges, combinations substitutions, replacements or other similar events.

2.3 Intentionally Omitted.

2.4 Intentionally Omitted.

2.5 No Fractional Share. No fractional Share shall be issuable upon exercise of this Warrant and the number of Shares to be issued shall be rounded down to the nearest whole Share. If a fractional Share interest arises upon any exercise of the Warrant, the Company shall eliminate such fractional Share interest by paying Holder in cash the amount computed by multiplying the fractional interest by (i) the fair market value (as determined in accordance with Section 1.3 above) of a full Share, less (ii) the then-effective Warrant Price.

2.6 Notice/Certificate as to Adjustments. Upon each adjustment of the Warrant Price, Common Stock and/or number of Shares, the Company, at the Company's expense, shall notify Holder in writing within a reasonable time setting forth the adjustments to the Warrant Price, class and/or number of Shares and facts upon which such adjustment is based. The Company shall, upon written request from Holder, furnish Holder with a certificate of its Chief Financial Officer, including computations of such adjustment and the Warrant Price, class and number of Shares in effect upon the date of such adjustment.

SECTION 3. REPRESENTATIONS AND COVENANTS OF THE COMPANY.

3.1 Representations and Warranties. The Company represents and warrants to, and agrees with, the Holder that all Shares which may be issued upon the exercise of this Warrant, shall, upon issuance, be duly authorized, validly issued, fully paid and non-assessable, and free of any liens and encumbrances except for restrictions on transfer provided for herein or under applicable federal and state securities laws. The Company covenants that it shall at all times cause to be reserved and kept available out of its authorized and unissued capital stock such number of securities as will be sufficient to permit the exercise in full of this Warrant.

3.2 Notice of Certain Events. If the Company proposes at any time to:

(a) declare any dividend or distribution upon the outstanding shares of the Company's stock, whether in cash, property, stock, or other securities and whether or not a regular cash dividend;

(b) offer for subscription or sale pro rata to the holders of the outstanding shares any additional shares of any class or series of the Company's stock (other than pursuant to contractual pre-emptive rights);

(c) effect any reclassification, exchange, combination, substitution, reorganization or recapitalization of the outstanding shares of the Common Stock; or

(d) effect an Acquisition or to liquidate, dissolve or wind up; then, in connection with each such event, the Company shall give Holder notice thereof at the same time and in the same manner as given to holders of the outstanding shares of the Common Stock.

SECTION 4. REPRESENTATIONS, WARRANTIES OF THE HOLDER.

The Holder represents and warrants to the Company as follows:

4.1 Purchase for Own Account. This Warrant and the Shares to be acquired upon exercise of this Warrant by Holder are being acquired for investment for Holder's account, not as a nominee or agent, and not with a view to the public resale or distribution within the meaning of the Act. Holder also represents that it has not been formed for the specific purpose of acquiring this Warrant or the Shares.

4.2 Disclosure of Information. Holder is aware of the Company's business affairs and financial condition and has received or has had full access to all the information it considers necessary or appropriate to make an informed investment decision with respect to the acquisition of this Warrant and its underlying securities. Holder further has had an opportunity to ask questions and receive answers from the Company regarding the terms and conditions of the offering of this Warrant and its underlying securities and to obtain additional information (to the extent the Company possessed such information or could acquire it without unreasonable effort or expense) necessary to verify any information furnished to Holder or to which Holder has access.

4.3 Investment Experience. Holder understands that the purchase of this Warrant and its underlying securities involves substantial risk. Holder has experience as an investor in securities of companies in the development stage and acknowledges that Holder can bear the economic risk of such Holder's investment in this Warrant and its underlying securities and has such knowledge and experience in financial or business matters that Holder is capable of evaluating the merits and risks of its investment in this Warrant and its underlying securities and/or has a preexisting personal or business relationship with the Company and certain of its officers, directors or controlling persons of a nature and duration that enables Holder to be aware of the character, business acumen and financial circumstances of such persons.

4.4 Accredited Investor Status. Holder is an "accredited investor" within the meaning of Regulation D promulgated under the Act.

4.5 The Act. Holder understands that this Warrant and the Shares issuable upon exercise hereof have not been registered under the Act in reliance upon a specific exemption therefrom, which exemption depends upon, among other things, the bona fide nature of the Holder's investment intent and the accuracy of the Holder's representations and warranties as expressed herein. Holder understands that this Warrant and the Shares issued upon any exercise hereof must be held indefinitely unless subsequently registered under the Act and qualified under applicable state securities laws, or unless exemption from such registration and qualification are otherwise available. Holder is aware of the provisions of Rule 144 promulgated under the Act.

4.6 No Shareholder Rights. Without limiting any provision of this Warrant, Holder agrees that as a Holder of this Warrant it will not have any rights (including, but not limited to, voting rights) as a shareholder of the Company with respect to the Shares issuable hereunder unless and until the exercise of this Warrant and then only with respect to the Shares issued on such exercise.

SECTION 5. MISCELLANEOUS.

5.1 Term and Automatic Cashless Exercise Upon Expiration.

(a) Term. Subject to the provisions of Section 1.6 above, this Warrant is exercisable in whole or in part at any time and from time to time on or before 6:00 PM, Pacific time, on the Expiration Date and shall be void thereafter.

(b) Automatic Cashless Exercise upon Expiration. In the event that, upon the Expiration Date, the fair market value of one Share (or other security issuable upon the exercise hereof) as determined in accordance with Section 1.3 above is greater than the Warrant Price in effect on such date, then this Warrant shall automatically be deemed on and as of such date to be exercised pursuant to Section 1.2 above as to all Shares (or such other securities) for which it shall not previously have been exercised, and the Company shall, within a reasonable time, cause its transfer agent and registrar to register in book-entry form, or to deliver to the Holder a certificate representing, the Shares (or such other securities) issued upon such exercise to Holder (which certificate may be in the form of an electronic certificate or DTC entry, to the extent used by the Company at the time of such exercise).

5.2 Legends. The Shares shall be imprinted with a legend in substantially the following form:

THE SHARES EVIDENCED BY THIS CERTIFICATE HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "ACT"), OR THE SECURITIES LAWS OF ANY STATE AND, EXCEPT AS SET FORTH IN THAT CERTAIN WARRANT TO PURCHASE COMMON STOCK ISSUED BY THE ISSUER TO WESTRIVER INNOVATION LENDING FUND VIII, L.P. DATED MARCH 25, 2019, MAY NOT BE OFFERED, SOLD, PLEDGED OR OTHERWISE TRANSFERRED UNLESS AND UNTIL REGISTERED UNDER SAID ACT AND LAWS OR, IN THE OPINION OF LEGAL COUNSEL IN FORM AND SUBSTANCE SATISFACTORY TO THE ISSUER, SUCH OFFER, SALE, PLEDGE OR OTHER TRANSFER IS EXEMPT FROM SUCH REGISTRATION.

5.3 Compliance with Securities Laws on Transfer. This Warrant and the Shares issuable upon exercise of this Warrant may not be transferred or assigned in whole or in part except in compliance with applicable federal and state securities laws by the transferor and the transferee (including, without limitation, the delivery of investment representation letters and legal opinions reasonably satisfactory to the Company, as reasonably requested by the Company). The Company shall not require Holder to provide an opinion of counsel if the transfer is to any affiliate of Holder, provided that any such transferee is an "accredited investor" as defined in Regulation D promulgated under the Act. Additionally, the Company shall also not require an opinion of counsel if there is no material question as to the availability of Rule 144 promulgated under the Act.

5.4 Transfer Procedure. Subject to the provisions of Section 5.3 and upon providing the Company with written notice, Holder and any subsequent Holder may transfer all or part of this Warrant or the Shares issuable upon exercise of this Warrant to any transferee, provided, however, in connection with any such transfer, Holder or any subsequent Holder will give the Company notice of the portion of the Warrant being transferred with the name, address and taxpayer identification number of the transferee and Holder will surrender this Warrant to the Company for reissuance to the transferee(s) (and Holder if applicable); and provided further, that any subsequent transferee shall agree in writing with the Company to be bound by all of the terms and conditions of this Warrant.

Notwithstanding anything to the contrary contained herein, so long as no Event of Default has occurred and is continuing, the Holder shall not transfer any portion of this Warrant to a direct competitor of the Company or a vulture fund, in each case as reasonably determined by the Holder, without the Company's consent, other than in connection with (x) assignments by the Holder due to a forced divestiture at the request of any regulatory agency, or (y) upon the occurrence of a default, event of default or similar occurrence with respect to the Holder's own financing or securitization transactions.

5.5 Notices. All notices and other communications hereunder from the Company to the Holder, or vice versa, shall be deemed delivered and effective (i) when given personally, (ii) on the third (3rd) Business Day after being mailed by first-class registered or certified mail, postage prepaid, (iii) upon actual receipt if given by facsimile or electronic mail and such receipt is confirmed in writing by the recipient, or (iv) on the first Business Day following delivery to a reliable overnight courier service, courier fee prepaid, in any case at such address as may have been furnished to the Company or Holder, as the case may be, in writing by the Company or such Holder from time to time in accordance with the provisions of this Section 5.5. All notices to Holder shall be addressed as follows until the Company receives notice of a change of address in connection with a transfer or otherwise:

Westriver Innovation Lending Fund VIII, L.P.
c/o WestRiver Mezzanine Loans, LLC
3720 Carillon Point
Kirkland, Washington 98033-7455
Attention: Harper Ellison
Telephone: (425) 952-3953
Email: Harper@wrg.vc

Notice to the Company shall be addressed as follows until Holder receives notice of a change in address:

PHASEBIO PHARMACEUTICALS, INC.
1 Great Valley Parkway, Suite 30
Malvern, PA 19355
Attn: Jonathan Mow, CEO
Email: jonathan.mow@phasebio.com

With a copy (which shall not constitute notice) to:

COOLEY LLP
Attn: Christian Plaza
11951 Freedom Drive, 14th Floor
Reston, VA 20190
Telephone: (703) 456-8006
Fax: (703) 456-8100
Email: cplaza@cooley.com

5.6 Waiver. This Warrant and any term hereof may be changed, waived, discharged or terminated (either generally or in a particular instance and either retroactively or prospectively) only by an instrument in writing signed by the party against which enforcement of such change, waiver, discharge or termination is sought.

5.7 Attorney's Fees. In the event of any dispute between the parties concerning the terms and provisions of this Warrant, the party prevailing in such dispute shall be entitled to collect from the other party all costs incurred in such dispute, including reasonable attorneys' fees.

5.8 Counterparts; Facsimile/Electronic Signatures. This Warrant may be executed in counterparts, all of which together shall constitute one and the same agreement. Any signature page delivered electronically or by facsimile shall be binding to the same extent as an original signature page with regards to any agreement subject to the terms hereof or any amendment thereto.

5.9 Governing Law. This Warrant shall be governed by and construed in accordance with the laws of the State of California, without giving effect to its principles regarding conflicts of law.

5.10 Headings. The headings in this Warrant are for purposes of reference only and shall not limit or otherwise affect the meaning of any provision of this Warrant.

5.11 Business Days. "**Business Day**" is any day that is not a Saturday, Sunday or a day on which Silicon Valley Bank is closed.

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IN WITNESS WHEREOF, the parties have caused this Warrant to Purchase Common Stock to be executed by their duly authorized representatives effective as of the Issue Date written above.

“COMPANY”

PHASEBIO PHARMACEUTICALS, INC.

By: /s/ Jonathan P. Mow

Name: Jonathan P. Mow

Title: CEO

“HOLDER”

WESTRIVER INNOVATION LENDING FUND VIII, L.P.

By: /s/ Trent Dawson

Trent Dawson, Chief Financial Officer

[Signature Page to Warrant to Purchase Common Stock]

APPENDIX 1

NOTICE OF EXERCISE

1. The undersigned Holder hereby exercises its right to purchase _____ shares of the Common Stock of **PHASEBIO PHARMACEUTICALS, INC.** (the “**Company**”) in accordance with the attached Warrant To Purchase Common Stock, and tenders payment of the aggregate Warrant Price for such shares as follows:

- check in the amount of \$_____ payable to order of the Company enclosed herewith
- Wire transfer of immediately available funds to the Company’s account
- Cashless Exercise pursuant to Section 1.2 of the Warrant
- Other [Describe] _____

2. Please issue a certificate or certificates representing the Shares in the name specified below:

Holder’s Name

(Address)

3. By its execution below and for the benefit of the Company, Holder hereby restates each of the representations and warranties in Section 4 of the Warrant to Purchase Common Stock as of the date hereof.

HOLDER:

By: _____

Name: _____

Title: _____

(Date): _____

LOAN AND SECURITY AGREEMENT

THIS LOAN AND SECURITY AGREEMENT (this “**Agreement**”) dated as of March 25, 2019 (the “**Effective Date**”) among (a) **SILICON VALLEY BANK**, a California corporation (“**SVB**” or “**Bank**”), in its capacity as administrative agent and collateral agent (“**Agent**”), (b) **SILICON VALLEY BANK**, a California corporation, as a lender, (c) **WESTRIVER INNOVATION LENDING FUND VIII, L.P.**, a Delaware limited partnership (“**WestRiver**”), as a lender (SVB and WestRiver and each of the other “**Lenders**” from time to time a party hereto are referred to herein collectively as the “**Lenders**” and each individually as a “**Lender**”), and (d) **PHASEBIO PHARMACEUTICALS, INC.**, a Delaware corporation (“**Borrower**”), provides the terms on which Agent and the Lenders shall lend to Borrower and Borrower shall repay Agent and the Lenders. The parties agree as follows:

1 ACCOUNTING AND OTHER TERMS

Accounting terms not defined in this Agreement shall be construed following GAAP. Calculations and determinations must be made following GAAP. Capitalized terms not otherwise defined in this Agreement shall have the meanings set forth in Section 14 of this Agreement. All other terms contained in this Agreement, unless otherwise indicated, shall have the meaning provided by the Code to the extent such terms are defined therein.

2 LOAN AND TERMS OF PAYMENT

2.1 Promise to Pay. Borrower hereby unconditionally promises to pay to Agent, for the ratable benefit of each Lender, the outstanding principal amount of all Credit Extensions advanced to Borrower by such Lender and accrued and unpaid interest thereon, together with any fees as and when due in accordance with this Agreement.

2.1.1 Growth Capital Advances

(a) Availability. Subject to the terms and conditions of this Agreement, the Lenders, severally and not jointly, agree to make growth capital advances to Borrower from time to time in three (3) tranches: “Tranche A”, “Tranche B” and “Tranche C”. On the Effective Date, or as soon thereafter as all conditions precedent to the making thereof have been met, the Lenders shall make one (1) growth capital advance under Tranche A to Borrower, in an amount equal to Seven Million Five Hundred Thousand Dollars (\$7,500,000) (the “**Tranche A Growth Capital Advance**”) according to each Lender’s Tranche A Loan Advance Commitment as set forth on Schedule 1.1 attached hereto, which shall be used to refinance all obligations owing from Borrower to Bank under the SVB Loan Agreement, and for working capital purposes. During the Tranche B Draw Period, Borrower may request and the Lenders shall make one (1) growth capital advance under Tranche B to Borrower, in an amount equal to Two Million Five Hundred Thousand Dollars (\$2,500,000) (the “**Tranche B Growth Capital Advance**”) according to each Lender’s Tranche B Loan Advance Commitment as set forth on Schedule 1.1 attached hereto. If Borrower achieves the Tranche C Milestone on or prior to December 31, 2019, Borrower shall, on or prior to the date that is ten (10) days after Borrower achieves the Tranche C Milestone, request and, provided no Event of Default has occurred and is continuing hereunder, the Lenders shall make one (1) growth capital advance under Tranche C to Borrower, in an amount equal to Five Million Dollars (\$5,000,000) (the “**Tranche C Growth Capital Advance**”, and together with the Tranche A Growth Capital Advance and the Tranche B Growth Capital Advance, each a “**Growth Capital Advance**” and collectively, the “**Growth Capital Advances**”) according to each Lender’s Tranche C Loan Advance Commitment as set forth on Schedule 1.1 attached hereto. The aggregate outstanding amount of the Growth Capital Advances shall not, at any time, exceed the Growth Capital Line. After repayment, no Growth Capital Advance (or any portion thereof) may be reborrowed.

(b) Interest Period. Commencing on the first (1st) Payment Date of the month following the month in which the Funding Date of the applicable Growth Capital Advance occurs, and continuing on the Payment Date of each month thereafter, Borrower shall make monthly payments of interest to Agent, for the account of the Lenders, in arrears, on the principal amount of each Growth Capital Advance, at the rate set forth in Section 2.2(a).

(c) Repayment. Commencing on the Amortization Start Date, and continuing on each Payment Date thereafter, Borrower shall repay the aggregate outstanding Growth Capital Advances to Agent, for the account of the Lenders, in (i) consecutive equal monthly installments of principal based on the Repayment Schedule, plus (ii) monthly payments of accrued interest at the rate set forth in Section 2.2(a). All outstanding principal and accrued and unpaid interest with respect to the Growth Capital Advances, and all other outstanding Obligations under the Growth Capital Advances, are due and payable in full on the Growth Capital Maturity Date.

(d) Permitted Prepayment. Borrower shall have the option to prepay all, but not less than all, of any Growth Capital Advances advanced by the Lenders under this Agreement, provided Borrower (i) provides written notice to Agent of its election to prepay such Growth Capital Advance at least ten (10) days prior to such prepayment, and (ii) pays to Agent, for the account of the Lenders in accordance with their respective Pro Rata Share, on the date of such prepayment (A) all outstanding principal plus accrued and unpaid interest in connection with the Growth Capital Advance being prepaid, (B) the applicable portion of the Prepayment Premium due in connection with the Growth Capital Advance being prepaid, (C) the applicable portion of the Final Payment due in connection with the Growth Capital Advance being prepaid, and (D) all other sums, if any, that shall have become due and payable, in connection with the Growth Capital Advance being prepaid, including Lenders' Expenses and interest at the Default Rate with respect to any past due amounts.

(e) Mandatory Prepayment Upon an Acceleration. If the Growth Capital Advances are accelerated by Agent pursuant to Section 9.1 hereof, following the occurrence of an Event of Default, Borrower shall immediately pay to Agent, for the account of the Lenders in accordance with its respective Pro Rata Share, an amount equal to the sum of (i) all outstanding principal plus accrued and unpaid interest with respect to the Growth Capital Advances, (ii) the Prepayment Premium, (iii) the Final Payment and (iv) all other sums, if any, that shall have become due and payable, including Lenders' Expenses and interest at the Default Rate with respect to any past due amounts.

2.2 Payment of Interest on the Credit Extensions.

(a) Interest Rate. Subject to Section 2.2(b), the principal amount outstanding under each Growth Capital Advance shall accrue interest at a floating per annum rate equal to the greater of (i) six and one-half of one percent (6.50%) and (ii) one percent (1.00%) above the Prime Rate, which interest, in each case, shall be payable monthly in accordance with Section 2.2(d) below.

(b) Default Rate. Immediately upon the occurrence and during the continuance of an Event of Default, Obligations shall bear interest at a rate per annum which is five percent (5.0%) above the rate that is otherwise applicable thereto (the "**Default Rate**"). Fees and expenses which are required to be paid by Borrower pursuant to the Loan Documents (including, without limitation, Lenders' Expenses) but are not paid when due shall bear interest until paid at a rate equal to the highest rate applicable to the Obligations. Payment or acceptance of the increased interest rate provided in this Section 2.2(b) is not a permitted alternative to timely payment and shall not constitute a waiver of any Event of Default or otherwise prejudice or limit any rights or remedies of Agent or any Lender.

(c) Adjustment to Interest Rate. Changes to the interest rate of any Credit Extension based on changes to the Prime Rate shall be effective on the effective date of any change to the Prime Rate and to the extent of any such change.

(d) Payment; Interest Computation. Interest is payable monthly on the Payment Date and shall be computed on the basis of a 360-day year for the actual number of days elapsed. In computing interest, (i) all payments received after 12:00 p.m. Eastern time on any day shall be deemed received at the opening of business on the next Business Day, and (ii) the date of the making of any Credit Extension shall be included and the date of payment shall be excluded; provided, however, that if any Credit Extension is repaid on the same day on which it is made, such day shall be included in computing interest on such Credit Extension.

2.3 Fees and Expenses. Borrower shall pay to Agent:

(a) Final Payment. The Final Payment, when due hereunder, to be shared between the Lenders pursuant to their respective Growth Capital Loan Commitment Percentages;

(b) Prepayment Premium. The Prepayment Premium, when due hereunder, to be shared between the Lenders pursuant to their respective Growth Capital Loan Commitment Percentages; provided that the Lenders shall waive the Prepayment Premium if Borrower refinances the Growth Capital Advances with any Lender;

(c) Lenders' Expenses. All Lenders' Expenses (including reasonable attorneys' fees and expenses for documentation and negotiation of this Agreement) incurred through and after the Effective Date, when due (or, if no stated due date, upon demand by Agent).

Unless otherwise provided in this Agreement or in a separate writing by Agent, Borrower shall not be entitled to any credit, rebate, or repayment of any fees earned by Agent or any Lender pursuant to this Agreement notwithstanding any termination of this Agreement or the suspension or termination of any Lender's obligation to make loans and advances hereunder. Agent may deduct amounts owing by Borrower under the clauses of this Section 2.2 pursuant to the terms of Section 2.4(e). Agent shall provide Borrower written notice of deductions made from the Designated Deposit Account pursuant to the terms of the clauses of this Section 2.3.

2.4 Payments; Pro Rata Treatment; Application of Payments; Debit of Accounts.

(a) All payments (including prepayments) to be made by Borrower under any Loan Document shall be made to Agent for the account of Lenders, in immediately available funds in Dollars, without setoff or counterclaim, before 12:00 p.m. Eastern time on the date when due. Agent shall distribute such payments to Lenders in like funds as set forth in Section 2.5. Payments of principal and/or interest received after 12:00 p.m. Eastern time are considered received at the opening of business on the next Business Day. When a payment is due on a day that is not a Business Day, the payment shall be due the next Business Day, and additional fees or interest, as applicable, shall continue to accrue until paid.

(b) Each borrowing by Borrower from Lenders hereunder shall be made according to the respective Growth Capital Loan Commitment Percentages of the relevant Lenders.

(c) Except as otherwise provided herein, each payment (including each prepayment) by Borrower on account of principal or interest on the Growth Capital Advances shall be applied according to each Lender's Pro Rata Share of the outstanding principal amount of the Growth Capital Advances. The amount of each principal prepayment of the Growth Capital Advances shall be applied to reduce the then remaining installments of the Growth Capital Advances based upon each Pro Rata Share of Growth Capital Advances.

(d) Agent has the exclusive right to determine the order and manner in which all payments with respect to the Obligations may be applied. Borrower shall have no right to specify the order or the accounts to which Agent shall allocate or apply any payments required to be made by Borrower to Agent or otherwise received by Agent or any Lender under this Agreement when any such allocation or application is not specified elsewhere in this Agreement.

(e) Agent may debit any of Borrower's deposit accounts, including the Designated Deposit Account, for principal and interest payments or any other amounts Borrower owes Agent or any Lender when due. These debits shall not constitute a set-off.

(f) Unless Agent shall have been notified in writing by Borrower prior to the date of any payment due to be made by Borrower hereunder that Borrower will not make such payment to Agent, Agent may assume that Borrower is making such payment, and Agent may, but shall not be required to, in reliance upon such assumption, make available to Lenders their respective Pro Rata Share of a corresponding payment amount. If such payment is not made to Agent by Borrower within three (3) Business Days after such due date, Agent shall be entitled to recover, on demand, from each Lender to which any amount which was made available pursuant to the preceding sentence, such amount with interest thereon at the rate per annum equal to the daily average Federal Funds Effective Rate. Nothing herein shall be deemed to limit the rights of Agent or any Lender against Borrower.

2.5 Settlement Procedures. If Agent receives any payment for the account of Lenders on or prior to 12:00 p.m. (Eastern time) on any Business Day, Agent shall pay to each applicable Lender such Lender's Pro Rata

Share of such payment on such Business Day. If Agent receives any payment for the account of Lenders after 12:00 p.m. (Eastern time) on any Business Day, Agent shall pay to each applicable Lender such Lender's Pro Rata Share of such payment on the next Business Day.

2.6 Withholding. Payments received by Agent from Borrower under this Agreement will be made free and clear of and without deduction for any and all present or future taxes, levies, imposts, duties, deductions, withholdings, assessments, fees or other charges imposed by any Governmental Authority (including any interest, additions to tax or penalties applicable thereto). Specifically, however, if at any time any Governmental Authority, applicable law, regulation or international agreement requires Borrower to make any withholding or deduction from any such payment or other sum payable hereunder to Agent, Borrower hereby covenants and agrees that the amount due from Borrower with respect to such payment or other sum payable hereunder will be increased to the extent necessary to ensure that, after the making of such required withholding or deduction, Agent receives a net sum equal to the sum which it would have received had no withholding or deduction been required, and Borrower shall pay the full amount withheld or deducted to the relevant Governmental Authority. Borrower will, upon request, furnish Agent with proof reasonably satisfactory to Agent indicating that Borrower has made such withholding payment; provided, however, that Borrower need not make any withholding payment if the amount or validity of such withholding payment is contested in good faith by appropriate and timely proceedings and as to which payment in full is bonded or reserved against by Borrower. The agreements and obligations of Borrower contained in this Section 2.6 shall survive the termination of this Agreement.

3 CONDITIONS OF LOANS

3.1 Conditions Precedent to Initial Credit Extension. Each Lender's obligation to make the initial Credit Extension hereunder is subject to the condition precedent that Agent shall have received, in form and substance satisfactory to Agent and the Lenders, such documents, and completion of such other matters, as Agent may reasonably deem necessary or appropriate, including, without limitation:

- (a) duly executed original signatures to the Loan Documents;
- (b) duly executed original signatures to a Warrant to Purchase Common Stock issued by Borrower in favor of Bank;
- (c) duly executed original signatures to a Warrant to Purchase Common Stock issued by Borrower in favor of WestRiver;
- (d) the Operating Documents and long-form good standing certificates of Borrower certified by the Secretary of State of the State of Delaware each other jurisdiction in which Borrower is qualified to conduct business, each dated as of a date no earlier than thirty (30) days prior to the Effective Date;
- (e) duly executed signatures to the completed Borrowing Resolutions for Borrower;
- (f) certified copies, dated as of a recent date, of Lien searches (including without limitation, UCC searches), as Agent may request, accompanied by written evidence (including any UCC termination statements and other Lien releases) that the Liens indicated in any such financing statements or other filings either constitute Permitted Liens or have been or, in connection with the initial Credit Extension hereunder, will be terminated or released;
- (g) the Perfection Certificate of Borrower, together with the duly executed signatures thereto;
- (h) a payoff letter from SVB with respect to all amounts owing from Borrower to Bank under the SVB Loan Agreement;
- (i) with respect to the Tranche B Growth Capital Advance only, an additional Warrant to Purchase Common Stock issued by Borrower in favor of each of (A) Bank and (B) WestRiver, in the form attached hereto as Annex I;

(j) with respect to the Tranche C Growth Capital Advance only, an additional Warrant to Purchase Common Stock issued by Borrower in favor of each of (A) Bank and (B) WestRiver, in substantially the form attached hereto as Annex I; and

(k) payment of the fees and Lenders' Expenses then due as specified in Section 2.3 hereof.

3.2 Conditions Precedent to all Credit Extensions. Each Lender's obligation to make each Credit Extension, including the initial Credit Extension, is subject to the following conditions precedent:

(a) timely receipt by the Lenders of (i) an executed Disbursement Letter and (ii) an executed Payment/Advance Form;

(b) the representations and warranties in this Agreement shall be true, accurate, and complete in all material respects on the date of the Disbursement Letter (and the Payment/Advance Form) and on the Funding Date of each Credit Extension; provided, however, that such materiality qualifier shall not be applicable to any representations and warranties that already are qualified or modified by materiality in the text thereof; and provided, further that those representations and warranties expressly referring to a specific date shall be true, accurate and complete in all material respects as of such date, and no Event of Default shall have occurred and be continuing or result from the Credit Extension. Each Credit Extension is Borrower's representation and warranty on that date that the representations and warranties in this Agreement remain true, accurate, and complete in all material respects; provided, however, that such materiality qualifier shall not be applicable to any representations and warranties that already are qualified or modified by materiality in the text thereof; and provided, further that those representations and warranties expressly referring to a specific date shall be true, accurate and complete in all material respects as of such date; and

(c) Agent and each Lender determine to its satisfaction that there has not been a Material Adverse Change.

3.3 Covenant to Deliver. Borrower agrees to deliver to Agent and each Lender each item required to be delivered to Agent and each Lender under this Agreement as a condition precedent to any Credit Extension. Borrower expressly agrees that a Credit Extension made prior to the receipt by Agent and each Lender of any such item shall not constitute a waiver by Agent or Lenders of Borrower's obligation to deliver such item, and the making of any Credit Extension in the absence of a required item shall be in each Lender's sole discretion.

3.4 Procedures for Borrowing.

(a) Growth Capital Advances. Subject to the prior satisfaction of all other applicable conditions to the making of a Credit Extension set forth in this Agreement, to obtain a Credit Extension, Borrower shall notify Agent (which notice shall be irrevocable) by electronic mail, facsimile, or telephone by 12:00 p.m. Eastern time at least five (5) Business Days before the proposed Funding Date of such Credit Extension. Together with any such electronic or facsimile notification, Borrower shall deliver to Agent by electronic mail or facsimile a completed Disbursement Letter (and Payment/Advance Form) executed by an Authorized Signer. Agent may rely on any telephone notice given by a person whom Agent believes is an Authorized Signer. On the Funding Date, Agent shall credit the Credit Extensions to the Designated Deposit Account. Agent may make Credit Extensions under this Agreement based on instructions from an Authorized Signer or without instructions if the Credit Extensions are necessary to meet Obligations which have become due

(b) Funding. In determining compliance with any condition hereunder to the making of a Credit Extension that, by its terms, must be fulfilled to the satisfaction of a Lender, Agent may presume that such condition is satisfactory to such Lender unless Agent shall have received notice to the contrary from such Lender prior to the making of such Credit Extension. Unless Agent shall have been notified in writing by any Lender prior to the date of any Credit Extension, that such Lender will not make the amount that would constitute its share of such borrowing available to Agent, Agent may assume that such Lender is making such amount available to Agent, and Agent may, in reliance upon such assumption, make available to Borrower a corresponding amount. If such amount is not made available to Agent by the required time on the Funding Date therefor, such Lender shall pay to Agent, on

demand, such amount with interest thereon, at a rate equal to the greater of (i) the Federal Funds Effective Rate or (ii) a rate determined by Agent in accordance with banking industry rules on interbank compensation, for the period until such Lender makes such amount immediately available to Agent. If such Lender's share of such Credit Extension is not made available to Agent by such Lender within three (3) Business Days after such Funding Date, Agent shall also be entitled to recover such amount with interest thereon at the rate per annum applicable to the Growth Capital Advances, on demand, from Borrower.

4 CREATION OF SECURITY INTEREST

4.1 Grant of Security Interest. Borrower hereby grants Agent, for the ratable benefit of the Lenders, to secure the payment and performance in full of all of the Obligations, a continuing security interest in, and pledges to Agent, for the ratable benefit of the Lenders, the Collateral, wherever located, whether now owned or hereafter acquired or arising, and all proceeds and products thereof. For clarity, any reference to "Agent's Lien" or any granting of collateral to Agent in this Agreement or any Loan Document means the Lien granted to Agent for the ratable benefit of the Lenders.

Borrower acknowledges that it previously has entered, and/or may in the future enter, into Bank Services Agreements with SVB. Regardless of the terms of any Bank Services Agreement, Borrower agrees that any amounts Borrower owes SVB thereunder shall be deemed to be Obligations hereunder and that it is the intent of Borrower and SVB to have all such Obligations secured by the first priority perfected security interest in the Collateral granted herein (subject only to Permitted Liens that are permitted pursuant to the terms of this Agreement to have superior priority to Agent's Lien in this Agreement), and by any and all other security agreements, mortgages or other collateral granted to Agent by Borrower as security for the Obligations, now or in the future.

If this Agreement is terminated, Agent's Lien in the Collateral shall continue until the Obligations (other than inchoate indemnity obligations) are repaid in full in cash. Upon payment in full in cash of the Obligations (other than inchoate indemnity obligations) and at such time as the Lenders' obligation to make Credit Extensions has terminated, Agent shall, at the sole cost and expense of Borrower, release its Liens in the Collateral and all rights therein shall revert to Borrower. In the event (x) all Obligations (other than inchoate indemnity obligations), except for Bank Services, are satisfied in full, and (y) this Agreement is terminated, Agent shall terminate the security interest granted herein upon Borrower providing to SVB cash collateral acceptable to SVB in its good faith business judgment for Bank Services, if any. In the event such Bank Services consist of outstanding Letters of Credit, Borrower shall provide to SVB cash collateral in an amount equal to (x) if such Letters of Credit are denominated in Dollars, then at least one hundred five percent (105.0%); and (y) if such Letters of Credit are denominated in a Foreign Currency, then at least one hundred ten percent (110.0%), of the Dollar Equivalent of the face amount of all such Letters of Credit plus, in each case, all interest, fees, and costs due or to become due in connection therewith (as estimated by SVB in its business judgment), to secure all of the Obligations relating to such Letters of Credit.

4.2 Priority of Security Interest. Borrower represents, warrants, and covenants that the security interests granted herein are and shall at all times continue to be first priority perfected security interests in the Collateral (subject only to Permitted Liens that are permitted pursuant to the terms of this Agreement to have superior priority to Agent's Lien under this Agreement). If Borrower shall acquire a commercial tort claim, Borrower shall promptly notify Agent in a writing signed by Borrower of the general details thereof and grant to Agent, for the ratable benefit of the Lenders, in such writing a security interest therein and in the proceeds thereof, all upon the terms of this Agreement, with such writing to be in form and substance reasonably satisfactory to Agent.

4.3 Authorization to File Financing Statements. Borrower hereby authorizes Agent, on behalf of the Lenders, to file financing statements and other similar forms, without notice to Borrower, with all appropriate jurisdictions to perfect or protect Agent's and Lenders' interest or rights hereunder, including a notice that any disposition of the Collateral, by either Borrower or any other Person, shall be deemed to violate the rights of Agent under the Code.

5 REPRESENTATIONS AND WARRANTIES

Borrower represents and warrants as follows:

5.1 Due Organization, Authorization; Power and Authority. Borrower is duly organized, validly existing, and in good standing as a Registered Organization in its jurisdiction of formation and is qualified and licensed to do business and is in good standing in any other jurisdiction in which the conduct of its business or its ownership of property and other assets or business which it is engaged in requires that it be qualified except where the failure to do so could not reasonably be expected to have a material adverse effect on Borrower's business. In connection with this Agreement, Borrower has delivered to Agent and each Lender a completed certificate signed by Borrower, entitled "**Perfection Certificate**" (collectively, the "**Perfection Certificate**"). Borrower represents and warrants to Agent and each Lender that: (a) Borrower's exact legal name is that indicated on the Perfection Certificate and on the signature page hereof; (b) Borrower is an organization of the type and is organized or incorporated in the jurisdiction set forth in the Perfection Certificate; (c) the Perfection Certificate accurately sets forth Borrower's organizational identification number or accurately states that Borrower has none; (d) the Perfection Certificate accurately sets forth Borrower's place of business, or, if more than one, its chief executive office as well as such Borrower's mailing address (if different than its chief executive office); (e) except as indicated on the Perfection Certificate, Borrower (and each of its predecessors) has not, in the past five (5) years, changed its jurisdiction of formation, organizational structure or type, or any organizational number assigned by its jurisdiction; and (f) all other information set forth on the Perfection Certificate pertaining to Borrower and each of its Subsidiaries is accurate and complete in all material respects (it being understood and agreed that Borrower may from time to time update certain information in the Perfection Certificate after the Effective Date to the extent permitted by one or more specific provisions in this Agreement). If Borrower is not now a Registered Organization but later becomes one, Borrower shall promptly notify Agent of such occurrence and provide Agent with Borrower's organizational identification number.

The execution, delivery and performance by Borrower of the Loan Documents to which it is a party have been duly authorized, and do not (i) conflict with any of Borrower's organizational documents, (ii) contravene, conflict with, constitute a default under or violate any material Requirement of Law, (iii) contravene, conflict or violate any applicable order, writ, judgment, injunction, decree, determination or award of any Governmental Authority by which Borrower or any of its Subsidiaries or any of their property or assets may be bound or affected, (iv) require any action by, filing, registration, or qualification with, or Governmental Approval from, any Governmental Authority (except such Governmental Approvals which have already been obtained and are in full force and effect and filings and registrations contemplated by this Agreement) or (v) conflict with, contravene, constitute a default or breach under, or result in or permit the termination or acceleration of, any material agreement by which Borrower is bound. Borrower is not in default under any agreement to which it is a party or by which it is bound in which the default could reasonably be expected to have a material adverse effect on Borrower's business.

5.2 Collateral. Borrower has good title to, rights in, and the power to transfer each item of the Collateral upon which it purports to grant a Lien under this Agreement and other Loan Documents, free and clear of any and all Liens except Permitted Liens. Borrower has no Collateral Accounts at or with any bank or financial institution other than SVB or SVB's Affiliates except for the Collateral Accounts described in the Perfection Certificate delivered to Agent and each Lender in connection herewith and which Borrower has given Agent notice and taken such actions as are necessary to give Agent, for the ratable benefit of the Lenders, a perfected security interest therein, pursuant to the terms of Section 6.6(b). The Accounts are bona fide, existing obligations of the Account Debtors.

The Collateral is not in the possession of any third party bailee (such as a warehouse) except as otherwise provided in the Perfection Certificate. None of the components of the Collateral shall be maintained at locations other than as provided in the Perfection Certificate or as permitted pursuant to Section 7.2.

All Inventory is in all material respects of good and marketable quality, free from material defects.

Borrower is the sole owner of the Intellectual Property which it owns or purports to own except for (a) non-exclusive licenses granted to its customers in the ordinary course of business, (b) over-the-counter software that is commercially available to the public, and (c) material Intellectual Property licensed to Borrower and noted on the Perfection Certificate. Each Patent which it owns or purports to own and which is material to Borrower's business is valid and enforceable, and no part of the Intellectual Property which Borrower owns or purports to own and which is material to Borrower's business has been judged invalid or unenforceable, in whole or in part. To the best of Borrower's knowledge, no claim has been made that any part of the Intellectual Property violates the rights of any third party except to the extent such claim would not reasonably be expected to have a material adverse effect on

Borrower's business. Except as noted on the Perfection Certificate, Borrower is not a party to, nor is it bound by, any Restricted License.

5.3 Litigation. There are no actions or proceedings pending or, to the knowledge of any Responsible Officer, threatened in writing by or against Borrower or any of its Subsidiaries reasonably expected to result in liability involving more than, individually or in the aggregate, Two Hundred Fifty Thousand Dollars (\$250,000.00).

5.4 Financial Statements; Financial Condition. All consolidated financial statements for Borrower and any of its Subsidiaries delivered to Agent and the Lenders fairly present in all material respects Borrower's consolidated financial condition and Borrower's consolidated results of operations. There has not been any material deterioration in Borrower's consolidated financial condition since the date of the most recent financial statements submitted to Agent and the Lenders.

5.5 Solvency. The fair salable value of Borrower's consolidated assets (including goodwill minus disposition costs) exceeds the fair value of Borrower's liabilities; Borrower is not left with unreasonably small capital after the transactions in this Agreement; and Borrower is able to pay its debts (including trade debts) as they mature.

5.6 Regulatory Compliance. Borrower is not an "investment company" or a company "controlled" by an "investment company" under the Investment Company Act of 1940, as amended. Borrower is not engaged as one of its important activities in extending credit for margin stock (under Regulations X, T and U of the Federal Reserve Board of Governors). Borrower (a) has complied in all material respects with all Requirements of Law, and (b) has not violated any Requirements of Law the violation of which could reasonably be expected to have a material adverse effect on its business. None of Borrower's or any of its Subsidiaries' properties or assets has been used by Borrower or any Subsidiary or, to the best of Borrower's knowledge, by previous Persons, in disposing, producing, storing, treating, or transporting any hazardous substance other than legally. Borrower and each of its Subsidiaries have obtained all consents, approvals and authorizations of, made all declarations or filings with, and given all notices to, all Governmental Authorities that are necessary to continue their respective businesses as currently conducted.

5.7 Subsidiaries; Investments. Borrower does not own any stock, partnership, or other ownership interest or other equity securities except for Permitted Investments.

5.8 Tax Returns and Payments; Pension Contributions. Borrower has timely filed all required tax returns and reports, and Borrower has timely paid all foreign, federal, state and local taxes, assessments, deposits and contributions owed by Borrower except (a) to the extent such taxes are being contested in good faith by appropriate proceedings promptly instituted and diligently conducted, so long as such reserve or other appropriate provision, if any, as shall be required in conformity with GAAP shall have been made therefor, or (b) if such taxes, assessments, deposits and contributions do not, individually or in the aggregate, exceed Fifty Thousand Dollars (\$50,000.00).

To the extent Borrower defers payment of any contested taxes, Borrower shall (i) notify Agent in writing of the commencement of, and any material development in, the proceedings and (ii) post bonds or take any other steps required to prevent the Governmental Authority levying such contested taxes from obtaining a Lien upon any of the Collateral that is other than a "Permitted Lien." Borrower is unaware of any claims or adjustments proposed for any of Borrower's prior tax years which could result in additional taxes becoming due and payable by Borrower in excess of Fifty Thousand Dollars (\$50,000.00). Borrower has paid all amounts necessary to fund all present pension, profit sharing and deferred compensation plans in accordance with their terms, and Borrower has not withdrawn from participation in, and has not permitted partial or complete termination of, or permitted the occurrence of any other event with respect to, any such plan which could reasonably be expected to result in any liability of Borrower, including any liability to the Pension Benefit Guaranty Corporation or its successors or any other governmental agency.

5.9 Use of Proceeds. Borrower shall use the proceeds of the Credit Extensions as working capital and to fund its general business requirements and not for personal, family, household or agricultural purposes.

5.10 Full Disclosure. No written representation, warranty or other statement of Borrower in any certificate or written statement given to Agent or any Lender in connection with the Loan Documents, or the

transactions contemplated thereby, as of the date such representation, warranty, or other statement was made, taken together with all such written certificates and written statements given to Agent or any Lender, contains any untrue statement of a material fact or omits to state a material fact necessary to make the statements contained in the certificates or statements not misleading (it being recognized by Agent and each Lender that the projections and forecasts provided by Borrower in good faith and based upon reasonable assumptions are not viewed as facts and that actual results during the period or periods covered by such projections and forecasts may differ from the projected or forecasted results).

5.11 Definition of “Knowledge.” For purposes of the Loan Documents, whenever a representation or warranty is made to Borrower’s knowledge or awareness, to the “best of” Borrower’s knowledge, or with a similar qualification, knowledge or awareness means the actual knowledge, after reasonable investigation, of any Responsible Officer.

6 AFFIRMATIVE COVENANTS

Borrower shall do all of the following:

6.1 Government Compliance.

(a) Maintain its and all its Subsidiaries’ legal existence and good standing in their respective jurisdictions of formation and maintain qualification in each jurisdiction in which the failure to so qualify would reasonably be expected to have a material adverse effect on Borrower’s business or operations. Borrower shall comply, and have each Subsidiary comply, in all material respects, with all laws, ordinances and regulations to which it is subject.

(b) Obtain all of the Governmental Approvals necessary for the performance by Borrower of its obligations under the Loan Documents to which it is a party and the grant of a security interest to Agent, for the ratable benefit of the Lenders, in all of its property. Borrower shall promptly provide copies of any such obtained Governmental Approvals to Agent.

6.2 Financial Statements, Reports, Certificates. Provide Agent and each Lender with the following:

(a) Monthly Financial Statements. As soon as available, but no later than thirty (30) days after the last day of each month, a company prepared consolidated and consolidating (if applicable) balance sheet, and income statement covering Borrower’s and each of its Subsidiary’s consolidated operations for such month certified by a Responsible Officer and in a form of presentation reasonably acceptable to Agent (the “**Monthly Financial Statements**”);

(b) Monthly Compliance Certificate. Within thirty (30) days after the last day of each month and together with the Monthly Financial Statements, a duly completed Compliance Certificate signed by a Responsible Officer, certifying that as of the end of such month, Borrower was in full compliance with all of the terms and conditions of this Agreement, and setting forth calculations showing compliance with the financial covenants (if any) set forth in this Agreement and such other information as Agent or the Lenders may reasonably request;

(c) Annual Operating Budget and Financial Projections. As soon as available, at least annually, but no later than sixty (60) days after each fiscal year end of Borrower and within thirty (30) days of any board-approved updates or amendments thereto, (i) annual operating budgets (including income statements, balance sheets and cash flow statements, by month) for such fiscal year of Borrower, and (ii) annual financial projections for such fiscal year (on a quarterly basis) as approved by Borrower’s board of directors, together with any related business forecasts used in the preparation of such annual financial projections;

(d) Annual Audited Financial Statements. As soon as available, but no later than within one hundred fifty (150) days after the last day of Borrower’s fiscal year, audited consolidated financial statements prepared under GAAP, consistently applied, together with an unqualified opinion on the financial statements from an independent certified public accounting firm reasonably acceptable to Agent;

(e) Other Statements. Within five (5) days of delivery, copies of all statements, reports and notices made available to Borrower's security holders or to any holders of Subordinated Debt;

(f) SEC Filings. Within five (5) days of filing, copies of all periodic and other reports, proxy statements and other materials filed by Borrower with the SEC, any Governmental Authority succeeding to any or all of the functions of the SEC or with any national securities exchange, or distributed to its shareholders, as the case may be. Documents required to be delivered pursuant to the terms hereof (to the extent any such documents are included in materials otherwise filed with the SEC) may be delivered electronically and if so delivered, shall be deemed to have been delivered on the date on which Borrower posts such documents, or provides a link thereto, on Borrower's website on the internet at Borrower's website address; provided, however, Borrower shall promptly notify Agent and the Lenders in writing (which may be by electronic mail) of the posting of any such documents;

(g) Legal Action Notice. A prompt report of any legal actions pending or threatened in writing against Borrower or any of its Subsidiaries that could reasonably be expected to result in damages or costs to Borrower or any of its Subsidiaries of, individually or in the aggregate, Two Hundred Fifty Thousand Dollars (\$250,000.00) or more; and

(h) Other Financial Information. Other financial information reasonably requested by Agent or any Lender.

6.3 Taxes; Pensions. (i) Timely file, and require each of its Subsidiaries to timely file, all required tax returns and reports and timely pay, and require each of its Subsidiaries to timely pay, all foreign, federal, state and local taxes, assessments, deposits and contributions owed by Borrower and each of its Subsidiaries, except for (x) deferred payment of any taxes contested pursuant to the terms of Section 5.8 hereof, and shall deliver to Agent, on demand, appropriate certificates attesting to such payments, and (ii) pay all amounts necessary to fund all present pension, profit sharing and deferred compensation plans in accordance with their terms.

6.4 Inventory; Returns. Keep all Inventory in good and marketable condition, free from material defects. Returns and allowances between Borrower and its Account Debtors shall follow Borrower's customary practices as they exist at the Effective Date. Borrower must promptly notify Agent and the Lenders of all returns, recoveries, disputes and claims that involve more than Two Hundred Fifty Thousand Dollars (\$250,000.00).

6.5 Insurance.

(a) Keep its business and the Collateral insured for risks and in amounts standard for companies in Borrower's industry and location and as Agent may reasonably request. Insurance policies shall be in a form, with financially sound and reputable insurance companies that are not Affiliates of Borrower, and in amounts that are satisfactory to Agent. All property policies shall have a lender's loss payable endorsement showing Agent as the sole lender loss payee. All liability policies shall show, or have endorsements showing, Agent as an additional insured. Agent shall be named as lender loss payee and/or additional insured with respect to any such insurance providing coverage in respect of any Collateral.

(b) Ensure that proceeds payable under any property policy are, at Agent's option, payable to Agent for the ratable benefit of the Lenders on account of the Obligations.

(c) At Agent's request, Borrower shall deliver certified copies of insurance policies and evidence of all premium payments. Each provider of any such insurance required under this Section 6.5 shall agree, by endorsement upon the policy or policies issued by it or by independent instruments furnished to Agent, that it will give Agent thirty (30) days prior written notice before any such policy or policies shall be materially altered or canceled. If Borrower fails to obtain insurance as required under this Section 6.5 or to pay any amount or furnish any required proof of payment to third persons and Agent, Agent may make all or part of such payment or obtain such insurance policies required in this Section 6.5, and take any action under the policies Agent deems prudent.

6.6 Operating Accounts.

(a) Maintain all of Borrower's and all of its Subsidiaries' operating, depository and securities/investment accounts with SVB and SVB's Affiliates. In addition, Borrower and any Guarantor shall use SVB's credit cards for all corporate credit card services and shall conduct all other primary banking with SVB for Bank Services.

(b) Provide Agent five (5) days prior written notice before establishing any Collateral Account at or with any bank or financial institution other than SVB or SVB's Affiliates. Borrower shall indicate in the Compliance Certificate provided to Agent in accordance with Section 6.2(b) above any deposit or securities account it holds at or with any bank or financial institution other than SVB or SVB's Affiliates and the aggregate value of deposits and/or securities in any such account. In addition, for each account that the Lenders in their sole discretion permit Borrower at any time to open or maintain (other than accounts at SVB), Borrower shall cause the applicable bank or financial institution (other than SVB) at or with which any such Collateral Account is opened or maintained to execute and deliver a Control Agreement or other appropriate instrument with respect to such Collateral Account to perfect Agent's Lien in such Collateral Account in accordance with the terms hereunder, which Control Agreement may not be terminated without the prior written consent of the Lenders. The provisions of the previous sentence shall not apply to deposit accounts exclusively used for payroll, payroll taxes and other employee wage and benefit payments to or for the benefit of Borrower's employees and identified to Agent and the Lenders by Borrower as such.

6.7 Protection of Intellectual Property Rights.

(a) (i) Protect, defend and maintain the validity and enforceability of any Intellectual Property; (ii) promptly advise Agent in writing of material infringements or any other event that could reasonably be expected to materially and adversely affect the value of its Intellectual Property; and (iii) not allow any Intellectual Property material to Borrower's business to be abandoned, forfeited or dedicated to the public without Agent's written consent.

(b) Provide written notice to Agent within ten (10) days of entering or becoming bound by any Restricted License (other than over-the-counter software that is commercially available to the public). Borrower shall take such steps as Agent requests to obtain the consent of, or waiver by, any person whose consent or waiver is necessary for (i) any Restricted License to be deemed "Collateral" and for Agent to have a security interest in it that might otherwise be restricted or prohibited by law or by the terms of any such Restricted License, whether now existing or entered into in the future, and (ii) Agent to have the ability in the event of a liquidation of any Collateral to dispose of such Collateral in accordance with Agent's and the Lenders' rights and remedies under this Agreement and the other Loan Documents.

6.8 Litigation Cooperation. From the date hereof and continuing through the termination of this Agreement, make available to Agent, without expense to Agent or any Lender, Borrower and its officers, employees and agents and Borrower's books and records, to the extent that Agent and/or the Lenders may deem them reasonably necessary to prosecute or defend any third-party suit or proceeding instituted by or against Agent and/or any Lender with respect to any Collateral or relating to Borrower.

6.9 Access to Collateral; Books and Records. Allow Agent or its agents, at reasonable times, on one (1) Business Days' notice (provided no notice is required if an Event of Default has occurred and is continuing), to inspect the Collateral and audit and copy Borrower's Books. Such inspections or audits shall be conducted no more often than once every twelve (12) months unless an Event of Default has occurred and is continuing in which case such inspections and audits shall occur as often as Agent shall determine is necessary. The foregoing inspections and audits shall be at Borrower's expense and the charge therefor shall be Two Thousand Dollars (\$2,000.00) per person per day (or such higher amount as shall represent Agent's then-current standard charge for the same), plus reasonable out-of-pocket expenses. In the event Borrower and Agent schedule an audit more than eight (8) days in advance, and Borrower cancels or reschedules the audit with less than eight (8) days written notice to Agent, then (without limiting any of Agent's or any Lender's rights or remedies) Borrower shall pay Agent a fee of Two Thousand Dollars (\$2,000.00) plus any out-of-pocket expenses incurred by Agent to compensate Agent for the anticipated costs and expenses of the cancellation or rescheduling.

6.10 Formation or Acquisition of Subsidiaries. Notwithstanding and without limiting the negative covenants contained in Sections 7.3 and 7.7 hereof, at the time that Borrower or any Guarantor forms any direct or indirect Subsidiary or acquires any direct or indirect Subsidiary after the Effective Date, Borrower and such Guarantor shall (a) cause such new Subsidiary to provide to Agent, for the benefit of the Lenders, a joinder to the Loan Agreement to cause such Subsidiary to become a co-borrower or Guarantor (as determined by the Lenders in their sole discretion) hereunder, together with such appropriate financing statements and/or Control Agreements, all in form and substance satisfactory to the Lenders (including being sufficient to grant Agent, for the benefit of the Lenders a first priority Lien (subject to Permitted Liens) in and to the assets of such newly formed or acquired Subsidiary), (b) provide to the Agent for the benefit of the Lenders appropriate certificates and powers and financing statements, pledging all of the direct or beneficial ownership interest in such new Subsidiary, in form and substance satisfactory to the Lenders, and (c) provide to the Lenders all other documentation in form and substance satisfactory to the Lenders, including one or more opinions of counsel satisfactory to the Lenders, which in their opinion is appropriate with respect to the execution and delivery of the applicable documentation referred to above. Any document, agreement, or instrument executed or issued pursuant to this Section 6.10 shall be a Loan Document.

6.11 Further Assurances. Execute any further instruments and take further action as Agent and the Lenders reasonably request to perfect or continue Agent's Lien in the Collateral or to effect the purposes of this Agreement. Deliver to Agent and the Lenders, within five (5) days after the same are sent or received, copies of all correspondence, reports, documents and other filings with any Governmental Authority regarding compliance with or maintenance of Governmental Approvals or Requirements of Law or that could reasonably be expected to have a material effect on any of the Governmental Approvals or otherwise on the operations of Borrower or any of its Subsidiaries.

7 NEGATIVE COVENANTS

Borrower shall not do any of the following without the prior written consent of the Lenders:

7.1 Dispositions. Convey, sell, lease, transfer, assign, or otherwise dispose of (collectively a "**Transfer**"), or permit any of its Subsidiaries to Transfer, all or any part of its business or property, except for Transfers (a) of Inventory in the ordinary course of business; (b) of worn-out or obsolete Equipment that is, in the reasonable judgment of Borrower, no longer economically practicable to maintain or useful in the ordinary course of business of Borrower; (c) consisting of Permitted Liens and Permitted Investments; (d) consisting of the sale or issuance of any stock of Borrower permitted under Section 7.2 of this Agreement; (e) consisting of Borrower's use or transfer of money or Cash Equivalents in a manner that is not prohibited by the terms of this Agreement or the other Loan Documents; and (f) of non-exclusive licenses for the use of the property of Borrower or its Subsidiaries in the ordinary course of business and licenses that could not result in a legal transfer of title of the licensed property but that may be exclusive in respects other than territory and that may be exclusive as to territory only as to discreet geographical areas outside of the United States.

7.2 Changes in Business, Management, Control, or Business Locations. (a) Engage in or permit any of its Subsidiaries to engage in any business other than the businesses currently engaged in by Borrower and such Subsidiary, as applicable, or reasonably related thereto; (b) liquidate or dissolve; (c) fail to provide notice to Agent and Lenders of any Key Person departing from or ceasing to be employed by Borrower within ten (10) Business Days after such Key Person's departure from Borrower; or (d) permit or suffer any Change in Control.

Borrower shall not, without at least ten (10) days prior written notice to Agent: (1) add any new offices or business locations, including warehouses (unless such new offices or business locations contain less than Two Hundred Fifty Thousand Dollars (\$250,000.00) in Borrower's assets or property) or deliver any portion of the Collateral valued, individually or in the aggregate, in excess of Two Hundred Fifty Thousand Dollars (\$250,000.00) to a bailee at a location other than to a bailee and at a location already disclosed in the Perfection Certificate, (2) change its jurisdiction of organization, (3) change its organizational structure or type, (4) change its legal name, or (5) change any organizational number (if any) assigned by its jurisdiction of organization. If Borrower intends to add any new offices or business locations, including warehouses, containing in excess of Two Hundred Fifty Thousand Dollars (\$250,000.00) of Borrower's assets or property, then Borrower will cause the landlord of any such new offices or business locations, including warehouses, to execute and deliver a landlord consent in form and substance satisfactory to Agent. If Borrower intends to deliver any portion of the Collateral valued, individually or in the aggregate, in

excess of Two Hundred Fifty Thousand Dollars (\$250,000.00) to a bailee, and Agent and such bailee are not already parties to a bailee agreement governing both the Collateral and the location to which Borrower intends to deliver the Collateral, then Borrower will cause such bailee to execute and deliver a bailee agreement in form and substance reasonably satisfactory to Agent.

7.3 Mergers or Acquisitions. Merge or consolidate, or permit any of its Subsidiaries to merge or consolidate, with any other Person, or acquire, or permit any of its Subsidiaries to acquire, all or substantially all of the capital stock or property of another Person (including, without limitation, by the formation of any Subsidiary). A Subsidiary may merge or consolidate into another Subsidiary or into Borrower.

7.4 Indebtedness. Create, incur, assume, or be liable for any Indebtedness, or permit any Subsidiary to do so, other than Permitted Indebtedness.

7.5 Encumbrance. Create, incur, allow, or suffer any Lien on any of its property, or assign or convey any right to receive income, including the sale of any Accounts, or permit any of its Subsidiaries to do so, except for Permitted Liens, permit any Collateral not to be subject to the first priority security interest granted herein, or enter into any agreement, document, instrument or other arrangement (except with or in favor of Agent, for the ratable benefit of the Lenders) with any Person which directly or indirectly prohibits or has the effect of prohibiting Borrower or any Subsidiary from assigning, mortgaging, pledging, granting a security interest in or upon, or encumbering any of Borrower's or any Subsidiary's Intellectual Property, except as is otherwise permitted in Section 7.1 hereof and the definition of "Permitted Liens" herein.

7.6 Maintenance of Collateral Accounts. Maintain any Collateral Account except pursuant to the terms of Section 6.6(b) hereof.

7.7 Distributions; Investments. (a) Pay any dividends or make any distribution or payment or redeem, retire or purchase any capital stock, provided that (i) Borrower may convert any of its convertible securities into other securities pursuant to the terms of such convertible securities or otherwise in exchange thereof; (ii) Borrower may pay dividends solely in common stock; and (iii) Borrower may repurchase the stock of former employees, officers, directors or consultants pursuant to stock repurchase agreements so long as an Event of Default does not exist at the time of such repurchase and would not exist after giving effect to such repurchase, provided that the aggregate amount of all such repurchases does not exceed Two Hundred Fifty Thousand Dollars (\$250,000.00) per fiscal year; or (b) directly or indirectly make any Investment (including, without limitation, by the formation of any Subsidiary) other than Permitted Investments, or permit any of its Subsidiaries to do so.

7.8 Transactions with Affiliates. Directly or indirectly enter into or permit to exist any material transaction with any Affiliate of Borrower, except for transactions that are in the ordinary course of Borrower's business, upon fair and reasonable terms that are no less favorable to Borrower than would be obtained in an arm's length transaction with a non-affiliated Person.

7.9 Subordinated Debt. (a) Make or permit any payment on any Subordinated Debt, except under the terms of the subordination, intercreditor, or other similar agreement to which such Subordinated Debt is subject, or (b) amend any provision in any document relating to the Subordinated Debt which would increase the amount thereof, provide for earlier or greater principal, interest, or other payments thereon, or adversely affect the subordination thereof to Obligations owed to Agent and the Lenders.

7.10 Compliance. Become an "investment company" or a company controlled by an "investment company", under the Investment Company Act of 1940, as amended, or undertake as one of its important activities extending credit to purchase or carry margin stock (as defined in Regulation U of the Board of Governors of the Federal Reserve System), or use the proceeds of any Credit Extension for that purpose; fail to (a) meet the minimum funding requirements of ERISA, (b) prevent a Reportable Event or Prohibited Transaction, as defined in ERISA, from occurring, or (c) comply with the Federal Fair Labor Standards Act, the failure of any of the conditions described in clauses (a) through (c) which could reasonably be expected to have a material adverse effect on Borrower's business; or violate any other law or regulation, if the violation could reasonably be expected to have a material adverse effect on Borrower's business, or permit any of its Subsidiaries to do so; withdraw or permit any Subsidiary to withdraw from participation in, permit partial or complete termination of, or permit the occurrence of any other event with

respect to, any present pension, profit sharing and deferred compensation plan which could reasonably be expected to result in any liability of Borrower, including any liability to the Pension Benefit Guaranty Corporation or its successors or any other governmental agency.

8 EVENTS OF DEFAULT

Any one of the following shall constitute an event of default (an “**Event of Default**”) under this Agreement:

8.1 Payment Default. Borrower fails to (a) make any payment of principal or interest on any Credit Extension when due, or (b) pay any other Obligations within three (3) Business Days after such Obligations are due and payable (which three (3) Business Day cure period shall not apply to payments due on the Growth Capital Maturity Date). During the cure period, the failure to make or pay any payment specified under clause (b) hereunder is not an Event of Default (but no Credit Extension will be made during the cure period);

8.2 Covenant Default.

(a) Borrower fails or neglects to perform any obligation in Sections 6.2, 6.3, 6.5, 6.6, 6.7(b), 6.9, or 6.10, or violates any covenant in Section 7; or

(b) Borrower fails or neglects to perform, keep, or observe any other term, provision, condition, covenant or agreement contained in this Agreement or any Loan Documents, and as to any default (other than those specified in this Section 8) under such other term, provision, condition, covenant or agreement that can be cured, has failed to cure the default within ten (10) days after the occurrence thereof; provided, however, that if the default cannot by its nature be cured within the ten (10) day period or cannot after diligent attempts by Borrower be cured within such ten (10) day period, and such default is likely to be cured within a reasonable time, then Borrower shall have an additional period (which shall not in any case exceed thirty (30) days) to attempt to cure such default, and within such reasonable time period the failure to cure the default shall not be deemed an Event of Default (but no Credit Extensions shall be made during such cure period). Cure periods provided under this section shall not apply, among other things, to financial covenants or any other covenants set forth in clause (a) above;

8.3 Material Adverse Change. A Material Adverse Change occurs;

8.4 Attachment; Levy; Restraint on Business.

(a) (i) The service of process seeking to attach, by trustee or similar process, any funds of Borrower or of any entity under the control of Borrower (including a Subsidiary), or (ii) a notice of lien or levy is filed against any of Borrower’s assets by any Governmental Authority, and the same under subclauses (i) and (ii) hereof are not, within ten (10) days after the occurrence thereof, discharged or stayed (whether through the posting of a bond or otherwise); provided, however, no Credit Extensions shall be made during any ten (10) day cure period; or

(b) (i) any material portion of Borrower’s assets is attached, seized, levied on, or comes into possession of a trustee or receiver, or (ii) any court order enjoins, restrains, or prevents Borrower from conducting all or any material part of its business;

8.5 Insolvency. (a) Borrower or any of its Subsidiaries is unable to pay its debts (including trade debts) as they become due or otherwise becomes insolvent; (b) Borrower or any of its Subsidiaries begins an Insolvency Proceeding; or (c) an Insolvency Proceeding is begun against Borrower or any of its Subsidiaries and is not dismissed or stayed within thirty (30) days (but no Credit Extensions shall be made while any of the conditions described in clause (a) exist and/or until any Insolvency Proceeding is dismissed);

8.6 Other Agreements. There is, under any agreement to which Borrower or any Guarantor is a party with a third party or parties, (a) any default resulting in a right by such third party or parties, whether or not exercised, to accelerate the maturity of any Indebtedness in an amount individually or in the aggregate in excess of Two Hundred Fifty Thousand Dollars (\$250,000.00); or (b) any breach or default by Borrower or Guarantor, the result of which could reasonably be expected to have a material adverse effect on Borrower’s or any Guarantor’s business;

8.7 Judgments; Penalties. One or more fines, penalties, or final judgments, orders or decrees for the payment of money in an amount, individually or in the aggregate, of at least Two Hundred Fifty Thousand Dollars (\$250,000.00) (not covered by independent third-party insurance as to which liability has been accepted by such insurance carrier) shall be rendered against Borrower by any Governmental Authority, and the same are not, within ten (10) days after the entry, assessment or issuance thereof, discharged, satisfied, or paid, or after execution thereof, stayed or bonded pending appeal, or such judgments are not discharged prior to the expiration of any such stay (provided that no Credit Extensions will be made prior to the satisfaction, payment, discharge, stay, or bonding of such fine, penalty, judgment, order or decree);

8.8 Misrepresentations. Borrower or any Person acting for Borrower makes any representation, warranty, or other statement now or later in this Agreement, any Loan Document or in any writing delivered to Agent or any Lender or to induce Agent or any Lender to enter this Agreement or any Loan Document, and such representation, warranty, or other statement is incorrect in any material respect when made;

8.9 Subordinated Debt. Any document, instrument, or agreement evidencing any Subordinated Debt shall for any reason be revoked or invalidated or otherwise cease to be in full force and effect, any Person shall be in breach thereof or contest in any manner the validity or enforceability thereof or deny that it has any further liability or obligation thereunder, or the Obligations shall for any reason be subordinated or shall not have the priority contemplated by this Agreement;

8.10 Guaranty. (a) Any guaranty of any Obligations terminates or ceases for any reason to be in full force and effect; (b) any Guarantor does not perform any obligation or covenant under any guaranty of the Obligations; (c) any circumstance described in Sections 8.3, 8.4, 8.5, 8.7, or 8.8 occurs with respect to any Guarantor, or (d) the death, liquidation, winding up, or termination of existence of any Guarantor; or (e) (i) a material impairment in the perfection or priority of Agent's Lien in the collateral provided by Guarantor or in the value of such collateral or (ii) a material adverse change in the general affairs, management, results of operation, condition (financial or otherwise) or the prospect of repayment of the Obligations occurs with respect to any Guarantor; or

8.11 Governmental Approvals. Any Governmental Approval shall have been (a) revoked, rescinded, suspended, modified in an adverse manner or not renewed in the ordinary course for a full term or (b) subject to any decision by a Governmental Authority that designates a hearing with respect to any applications for renewal of any of such Governmental Approval or that could result in the Governmental Authority taking any of the actions described in clause (a) above, and such decision or such revocation, rescission, suspension, modification or non-renewal (i) cause, or could reasonably be expected to cause, a Material Adverse Change, or (ii) adversely affects the legal qualifications of Borrower or any of its Subsidiaries to hold such Governmental Approval in any applicable jurisdiction and such revocation, rescission, suspension, modification or non-renewal could reasonably be expected to affect the status of or legal qualifications of Borrower or any of its Subsidiaries to hold any Governmental Approval in any other jurisdiction.

9 RIGHTS AND REMEDIES

9.1 Rights and Remedies. Upon the occurrence and during the continuance of an Event of Default, Agent, in accordance with the Lender Intercreditor Agreement or, if such rights and remedies are not addressed in the Lender Intercreditor Agreement, as directed by a majority of the Lenders, may, without notice or demand, do any or all of the following:

(a) declare all Obligations immediately due and payable (but if an Event of Default described in Section 8.5 occurs all Obligations are immediately due and payable without any action by Agent or any Lender);

(b) stop advancing money or extending credit for Borrower's benefit under this Agreement or under any other agreement among Borrower, Agent and/or any Lenders;

(c) demand that Borrower (i) deposit cash with SVB in an amount equal to at least (x) one hundred five percent (105.0%) of the Dollar Equivalent of the aggregate face amount of all Letters of Credit denominated in Dollars remaining undrawn, and (y) one hundred ten percent (110.0%) of the Dollar Equivalent of the

aggregate face amount of all Letters of Credit denominated in a Foreign Currency remaining undrawn (plus, in each case, all interest, fees, and costs due or to become due in connection therewith (as estimated by SVB in its good faith business judgment)), to secure all of the Obligations relating to such Letters of Credit, as collateral security for the repayment of any future drawings under such Letters of Credit, and Borrower shall forthwith deposit and pay such amounts, and (ii) pay in advance all letter of credit fees scheduled to be paid or payable over the remaining term of any Letters of Credit;

(d) terminate any FX Contracts;

(e) verify the amount of, demand payment of and performance under, and collect any Accounts and General Intangibles, settle or adjust disputes and claims directly with Account Debtors for amounts on terms and in any order that Agent and/or the Lenders consider advisable, and notify any Person owing Borrower money of Agent's security interest in such funds;

(f) make any payments and do any acts Agent or any Lender considers necessary or reasonable to protect the Collateral and/or its security interest in the Collateral. Borrower shall assemble the Collateral if Agent requests and make it available as Agent designates. Agent may enter premises where the Collateral is located, take and maintain possession of any part of the Collateral, and pay, purchase, contest, or compromise any Lien which appears to be prior or superior to its security interest or charges and pay all expenses incurred. Borrower grants Agent a license to enter and occupy any of its premises, without charge, to exercise any of Agent's rights or remedies;

(g) apply to the Obligations (i) any balances and deposits of Borrower it holds, or (ii) any amount held by Agent owing to or for the credit or the account of Borrower;

(h) ship, reclaim, recover, store, finish, maintain, repair, prepare for sale, advertise for sale, and sell the Collateral. Agent, for the benefit of the Lenders, is hereby granted a non-exclusive, royalty-free license or other right to use, without charge, Borrower's labels, Patents, Copyrights, mask works, rights of use of any name, trade secrets, trade names, Trademarks, and advertising matter, or any similar property as it pertains to the Collateral, in completing production of, advertising for sale, and selling any Collateral and, in connection with Agent's exercise of its rights under this Section, Borrower's rights under all licenses and all franchise agreements inure to Agent, for the ratable benefit of the Lenders;

(i) place a "hold" on any account maintained with Agent or Lenders and/or deliver a notice of exclusive control, any entitlement order, or other directions or instructions pursuant to any Control Agreement or similar agreements providing control of any Collateral;

(j) demand and receive possession of Borrower's Books; and

(k) exercise all rights and remedies available to Agent and the Lenders under the Loan Documents or at law or equity, including all remedies provided under the Code (including disposal of the Collateral pursuant to the terms thereof) or any other applicable law.

9.2 Power of Attorney. Borrower hereby irrevocably appoints Agent, for the benefit of the Lenders, as its lawful attorney-in-fact, exercisable upon the occurrence and during the continuance of an Event of Default, to: (a) endorse Borrower's name on any checks or other forms of payment or security; (b) sign Borrower's name on any invoice or bill of lading for any Account or drafts against Account Debtors; (c) settle and adjust disputes and claims about the Accounts directly with Account Debtors, for amounts and on terms Agent determines reasonable; (d) make, settle, and adjust all claims under Borrower's insurance policies; (e) pay, contest or settle any Lien, charge, encumbrance, security interest, and adverse claim in or to the Collateral, or any judgment based thereon, or otherwise take any action to terminate or discharge the same; and (f) transfer the Collateral into the name of Agent or a third party as the Code permits. Borrower hereby appoints Agent as its lawful attorney-in-fact to sign Borrower's name on any documents necessary to perfect or continue the perfection of Agent's security interest in the Collateral regardless of whether an Event of Default has occurred until all Obligations have been satisfied in full and Lenders are under no further obligation to make Credit Extensions hereunder. Agent's foregoing appointment as Borrower's attorney in

fact, and all of Agent's rights and powers, coupled with an interest, are irrevocable until all Obligations have been fully repaid and performed and each Lender's obligation to provide Credit Extensions terminates.

9.3 Protective Payments. If Borrower fails to obtain the insurance called for by Section 6.5 or fails to pay any premium thereon or fails to pay any other amount which Borrower is obligated to pay under this Agreement or any other Loan Document or which may be required to preserve the Collateral, Agent may obtain such insurance or make such payment, and all amounts so paid by Agent are Lenders' Expenses and immediately due and payable, bearing interest at the then highest rate applicable to the Obligations, and secured by the Collateral. Agent will make reasonable efforts to provide Borrower with notice of Agent obtaining such insurance at the time it is obtained or within a reasonable time thereafter. No payments by Agent are deemed an agreement to make similar payments in the future or Agent's or and Lenders' waiver of any Event of Default.

9.4 Application of Payments and Proceeds Upon Default. If an Event of Default has occurred and is continuing, Agent shall have the right to apply in any order any funds in its possession, whether from Borrower account balances, payments, proceeds realized as the result of any collection of Accounts or other disposition of the Collateral, or otherwise, to the Obligations. Agent shall pay any surplus to Borrower by credit to the Designated Deposit Account or to other Persons legally entitled thereto; Borrower shall remain liable to Agent and the Lenders for any deficiency. If Agent, directly or indirectly, enters into a deferred payment or other credit transaction with any purchaser at any sale of Collateral, Agent shall have the option, exercisable at any time, of either reducing the Obligations by the principal amount of the purchase price or deferring the reduction of the Obligations until the actual receipt by Agent of cash therefor.

9.5 Liability for Collateral. So long as Agent and Lenders comply with reasonable banking practices regarding the safekeeping of the Collateral in their possession or under the control of Agent and/or Lenders, Agent and Lenders shall not be liable or responsible for: (a) the safekeeping of the Collateral; (b) any loss or damage to the Collateral; (c) any diminution in the value of the Collateral; or (d) any act or default of any carrier, warehouseman, bailee, or other Person. Borrower bears all risk of loss, damage or destruction of the Collateral.

9.6 No Waiver; Remedies Cumulative. Agent's and any Lender's failure, at any time or times, to require strict performance by Borrower of any provision of this Agreement or any other Loan Document shall not waive, affect, or diminish any right of Agent or any Lender thereafter to demand strict performance and compliance herewith or therewith. No waiver hereunder shall be effective unless signed by the party granting the waiver and then is only effective for the specific instance and purpose for which it is given. Agent's and each Lender's rights and remedies under this Agreement and the other Loan Documents are cumulative. Agent and each Lender have all rights and remedies provided under the Code, by law, or in equity. Agent's or any Lender's exercise of one right or remedy is not an election and shall not preclude Agent or any Lender from exercising any other remedy under this Agreement or any other Loan Document or other remedy available at law or in equity, and Agent's or any Lender's waiver of any Event of Default is not a continuing waiver. Agent's or any Lender's delay in exercising any remedy is not a waiver, election, or acquiescence.

9.7 Demand Waiver. Borrower waives demand, notice of default or dishonor, notice of payment and nonpayment, notice of any default, nonpayment at maturity, release, compromise, settlement, extension, or renewal of accounts, documents, instruments, chattel paper, and guarantees held by Agent on which Borrower is liable.

10 AGENT

10.1 Appointment and Authority.

(a) Each Lender hereby irrevocably appoints SVB to act on its behalf as Agent hereunder and under the other Loan Documents and authorizes Agent to take such actions on its behalf and to exercise such powers as are delegated to Agent by the terms hereof or thereof, together with such actions and powers as are reasonably incidental thereto.

(b) The provisions of this Section 10 are solely for the benefit of Agent and Lenders, and Borrower shall not have rights as a third party beneficiary of any of such provisions. Notwithstanding any provision

to the contrary elsewhere in this Agreement, Agent shall not have any duties or responsibilities to any Lender or any other Person, except those expressly set forth herein, or any fiduciary relationship with any Lender, and no implied covenants, functions, responsibilities, duties, obligations or liabilities shall be read into this Agreement or any other Loan Document or otherwise exist against Agent.

10.2 Delegation of Duties. Agent may perform any and all of its duties and exercise its rights and powers hereunder or under any other Loan Document by or through any one or more sub-agents appointed by Agent. Agent and any such sub-agent may perform any and all of its duties and exercise its rights and powers by or through their respective Indemnified Persons. The exculpatory provisions of this Section 10.2 shall apply to any such sub-agent and to the Indemnified Persons of Agent and any such sub-agent, and shall apply to their respective activities in connection with the syndication of the credit facilities provided for herein as well as activities as Agent.

10.3 Exculpatory Provisions. Agent shall have no duties or obligations except those expressly set forth herein and in the other Loan Documents. Without limiting the generality of the foregoing, Agent shall not:

(a) be subject to any fiduciary, trust, agency or other similar duties, regardless of whether any Event of Default has occurred and is continuing;

(b) have any duty to take any discretionary action or exercise any discretionary powers, except discretionary rights and powers expressly contemplated hereby or by the other Loan Documents that Agent is required to exercise as directed in writing by the Lenders, as applicable; provided that Agent shall not be required to take any action that, in its opinion or the opinion of its counsel, may expose Agent to liability or that is contrary to any Loan Document or applicable law; and

(c) except as expressly set forth herein and in the other Loan Documents, have any duty to disclose, and Agent shall not be liable for the failure to disclose, any information relating to Borrower or any of its Affiliates that is communicated to or obtained by any Person serving as Agent or any of its Affiliates in any capacity.

Agent shall not be liable for any action taken or not taken by it (i) with the consent or at the request of the Lenders (or as Agent shall believe in good faith shall be necessary, under the circumstances as provided in Section 13.7) or (ii) in the absence of its own gross negligence or willful misconduct.

Agent shall not be responsible for or have any duty to ascertain or inquire into (i) any statement, warranty or representation made in or in connection with this Agreement or any other Loan Document, (ii) the contents of any certificate, report or other document delivered hereunder or thereunder or in connection herewith or therewith, (iii) the performance or observance of any of the covenants, agreements or other terms or conditions set forth herein or therein or the occurrence of any Event of Default, (iv) the validity, enforceability, effectiveness or genuineness of this Agreement, any other Loan Document or any other agreement, instrument or document or (v) the satisfaction of any condition set forth in Section 3 or elsewhere herein, other than to confirm receipt of items expressly required to be delivered to Agent.

10.4 Reliance by Agent. Agent shall be entitled to rely upon, and shall not incur any liability for relying upon, any notice, request, certificate, consent, statement, instrument, document or other writing (including any electronic message, internet or intranet website posting or other distribution) believed by it to be genuine and to have been signed, sent or otherwise authenticated by the proper Person. Agent also may rely upon any statement made to it orally or by telephone and believed by it to have been made by the proper Person, and shall not incur any liability for relying thereon. Agent may consult with legal counsel (who may be counsel for Borrower), independent accountants and other experts selected by it, and shall not be liable for any action taken or not taken by it in accordance with the advice of any such counsel, accountants or experts. In determining compliance with any condition hereunder to the making of a Credit Extension that, by its terms, must be fulfilled to the satisfaction of a Lender, Agent may presume that such condition is satisfactory to such Lender unless Agent shall have received notice to the contrary from such Lender prior to the making of such Credit Extension. Agent shall in all cases be fully protected in acting, or in refraining from acting, under this Agreement and the other Loan Documents in accordance with a request of the Lenders, and such request and any action taken or failure to act pursuant thereto shall be binding upon Lenders and all future holders of the Credit Extensions.

10.5 Notice of Default. Agent shall not be deemed to have knowledge or notice of the occurrence of any Event of Default (except with respect to defaults in the payment of principal, interest or fees required to be paid to Agent for the account of Lenders), unless Agent has received notice from a Lender or Borrower referring to this Agreement, describing such Event of Default and stating that such notice is a “notice of default”. In the event that Agent receives such a notice, Agent shall give notice thereof to Lenders. Agent shall take such action with respect to such Event of Default as shall be reasonably directed by the Lenders.

10.6 Non-Reliance on Agent and Other Lenders. Each Lender expressly acknowledges that neither Agent nor any of its officers, directors, employees, agents, attorneys in fact or affiliates has made any representations or warranties to it and that no act by Agent hereafter taken, including any review of the affairs of a Group Member or any Affiliate of a Group Member, shall be deemed to constitute any representation or warranty by Agent to any Lender. Each Lender represents to Agent that it has, independently and without reliance upon Agent or any other Lender, and based on such documents and information as it has deemed appropriate, made its own appraisal of, and investigation into, the business, operations, property, financial and other condition and creditworthiness of the Group Members and their Affiliates and made its own decision to make its Credit Extensions hereunder and enter into this Agreement. Each Lender also represents that it will, independently and without reliance upon Agent or any other Lender, and based on such documents and information as it shall deem appropriate at the time, continue to make its own credit analysis, appraisals and decisions in taking or not taking action under this Agreement and the other Loan Documents, and to make such investigation as it deems necessary to inform itself as to the business, operations, property, financial and other condition and creditworthiness of the Group Members and their Affiliates. Except for notices, reports and other documents expressly required to be furnished to Lenders by Agent hereunder, Agent shall have no duty or responsibility to provide any Lender with any credit or other information concerning the business, operations, property, condition (financial or otherwise), prospects or creditworthiness of any Group Member or any Affiliate of a Group Member that may come into the possession of Agent or any of its officers, directors, employees, agents, attorneys in fact or Affiliates.

10.7 Indemnification. Each Lender agrees to indemnify Agent in its capacity as such (to the extent not reimbursed by Borrower and without limiting the obligation of Borrower to do so in accordance with the terms hereof, according to its Growth Capital Loan Commitment Percentage in effect on the date on which indemnification is sought under this Section 10.7 (or, if indemnification is sought after the date upon which the Commitments shall have terminated and the Obligations shall have been paid in full, in accordance with its Growth Capital Loan Commitment Percentage immediately prior to such date), from and against any and all liabilities, obligations, losses, damages, penalties, actions, judgments, suits, costs, expenses or disbursements of any kind whatsoever that may at any time (whether before or after the payment of the Credit Extensions) be imposed on, incurred by or asserted against Agent in any way relating to or arising out of, the Commitments, this Agreement, any of the other Loan Documents or any documents contemplated by or referred to herein or therein or the transactions contemplated hereby or thereby or any action taken or omitted by Agent under or in connection with any of the foregoing; provided that no Lender shall be liable for the payment of any portion of such liabilities, obligations, losses, damages, penalties, actions, judgments, suits, costs, expenses or disbursements that are found by a final and nonappealable decision of a court of competent jurisdiction to have resulted primarily from Agent’s gross negligence or willful misconduct. The agreements in this Section shall survive the payment of the Credit Extensions and all other amounts payable hereunder.

10.8 Agent in Its Individual Capacity. The Person serving as Agent hereunder shall have the same rights and powers in its capacity as a Lender as any other Lender and may exercise the same as though it were not Agent and the term “Lender” or “Lenders” shall, unless otherwise expressly indicated or unless the context otherwise requires, include each such Person serving as Agent hereunder in its individual capacity. Such Person and its Affiliates may accept deposits from, lend money to, act as the financial advisor or in any other advisory capacity for and generally engage in any kind of business with Borrower, any Guarantor or any Subsidiary or other Affiliate thereof as if such Person were not Agent hereunder and without any duty to account therefor to Lenders.

10.9 Successor Agent. Agent may at any time give notice of its resignation to Lenders and Borrower, which resignation shall not be effective until the time at which the majority of the Lenders have delivered to Agent their written consent to such resignation. Upon receipt of any such notice of resignation, the Lenders shall have the right, in consultation with Borrower, to appoint a successor, which shall be a financial institution with an office in the State of California, or an Affiliate of any such bank with an office in the State of California. If no such successor shall have been so appointed by the Lenders and shall have accepted such appointment within thirty (30) days after the

retiring Agent has received the written consent of the majority of the Lenders to such resignation, then the retiring Agent may on behalf of Lenders, appoint a successor Agent meeting the qualifications set forth above; provided that in no event shall any such successor Agent be a Defaulting Lender and provided further that if the retiring Agent shall notify Borrower and Lenders that no qualifying Person has accepted such appointment, then such resignation shall nonetheless become effective in accordance with such notice and (1) the retiring Agent shall be discharged from its duties and obligations hereunder and under the other Loan Documents (except that in the case of any collateral security held by Agent on behalf of the Lenders under any of the Loan Documents, the retiring Agent shall continue to hold such collateral security until such time as a successor Agent is appointed and such collateral security is assigned to such successor Agent) and (2) all payments, communications and determinations provided to be made by, to or through Agent shall instead be made by or to each Lender directly, until such time as the Lenders appoint a successor Agent as provided for above in this Section 10.9. Upon the acceptance of a successor's appointment as Agent hereunder, such successor shall succeed to and become vested with all of the rights, powers, privileges and duties of the retiring (or retired) Agent, and the retiring Agent shall be discharged from all of its duties and obligations hereunder or under the other Loan Documents (if not already discharged therefrom as provided above in this Section 10.9). The fees payable by Borrower to a successor Agent shall be the same as those payable to its predecessor unless otherwise agreed between the Borrower and such successor. After the retiring Agent's resignation hereunder and under the other Loan Documents, the provisions of this Section 10 shall continue in effect for the benefit of such retiring Agent, its sub-agents and their respective Indemnified Persons in respect of any actions taken or omitted to be taken by any of them while the retiring Agent was acting as Agent.

10.10 Defaulting Lender.

(a) Defaulting Lender Adjustments. Notwithstanding anything to the contrary contained in this Agreement, if any Lender becomes a Defaulting Lender, then, until such time as such Lender is no longer a Defaulting Lender, to the extent permitted by applicable law:

(i) Waivers and Amendments. Such Defaulting Lender's right to approve or disapprove any amendment, waiver or consent with respect to this Agreement shall be restricted as long as said Lender is a Defaulting Lender.

(ii) Defaulting Lender Waterfall. Any payment of principal, interest, fees or other amounts received by the Agent for the account of such Defaulting Lender (whether voluntary or mandatory, at maturity, pursuant to Section 8 or otherwise, and including any amounts made available to the Agent by such Defaulting Lender pursuant to Section 13.11), shall be applied at such time or times as may be determined by the Agent as follows: first, to the payment of any amounts owing by such Defaulting Lender to the Agent hereunder; second, as the Borrower may request (so long as no Event of Default exists), to the funding of any Growth Capital Advance in respect of which such Defaulting Lender has failed to fund its portion thereof as required by this Agreement, as determined by the Agent; third, if so determined by the Agent and Borrower, to be held in a Deposit Account and released pro rata to satisfy such Defaulting Lender's potential future funding obligations with respect to Growth Capital Advances under this Agreement; fourth, so long as no Event of Default has occurred and is continuing, to the payment of any amounts owing to the Borrower as a result of any judgment of a court of competent jurisdiction obtained by the Borrower against such Defaulting Lender as a result of such Defaulting Lender's breach of its obligations under this Agreement; and fifth, to such Defaulting Lender or as otherwise directed by a court of competent jurisdiction; provided that if (A) such payment is a payment of the principal amount of any Growth Capital Advances in respect of which such Defaulting Lender has not fully funded its appropriate share and (B) such Growth Capital Advances were made at a time when the conditions set forth in Section 3.1 were satisfied or waived, such payment shall be applied solely to pay the Loans of all non-Defaulting Lenders on a *pro rata* basis prior to being applied to the payment of any Growth Capital Advances of such Defaulting Lender until such time as all Growth Capital Advances are held by the Lenders pro rata in accordance with the Growth Capital Commitments under this Agreement. Any payments, prepayments or other amounts paid or payable to a Defaulting Lender that are applied (or held) to pay amounts owed by a Defaulting Lender pursuant to this Section 10.10(a)(ii) shall be deemed paid to and redirected by such Defaulting Lender, and each Lender irrevocably consents hereto.

(iii) Certain Fees. No Defaulting Lender shall be entitled to receive any fee pursuant to Section 2.3(b) or Section 2.3(c) for any period during which such Lender is a Defaulting Lender (and the Borrower shall not be required to pay any such fee that otherwise would have been required to have been paid to such Defaulting Lender).

(b) Defaulting Lender Cure. If Borrower and Agent agree in writing that a Lender is no longer a Defaulting Lender, Agent will so notify the parties hereto, whereupon as of the effective date specified in such notice and subject to any conditions set forth therein, such Lender will, to the extent applicable, purchase at par that portion of outstanding Growth Capital Advances of the other Lenders or take such other actions as Agent may determine to be necessary to cause the Growth Capital Advances to be held on a *pro rata* basis by the Lenders in accordance with their respective Growth Capital Loan Commitment Percentages, whereupon such Lender will cease to be a Defaulting Lender; provided that no adjustments will be made retroactively with respect to fees accrued or payments made by or on behalf of Borrower while such Lender was a Defaulting Lender; and provided further that, except to the extent otherwise expressly agreed by the affected parties, no change hereunder from Defaulting Lender to Lender will constitute a waiver or release of any claim of any party hereunder arising from such Lender having been a Defaulting Lender.

(c) Termination of Defaulting Lender. The Borrower may terminate the unused amount of the Growth Capital Commitment of any Lender that is a Defaulting Lender upon not less than ten (10) Business Days' prior notice to Agent (which shall promptly notify the Lenders thereof), and in such event the provisions of Section 10.10(a)(ii) will apply to all amounts thereafter paid by Borrower for the account of such Defaulting Lender under this Agreement (whether on account of principal, interest, fees, indemnity or other amounts); provided that (i) no Event of Default shall have occurred and be continuing, and (ii) such termination shall not be deemed to be a waiver or release of any claim Borrower, Agent or any Lender may have against such Defaulting Lender.

(d) If the Person serving as Agent is a Defaulting Lender pursuant to clause (d) of the definition thereof, the non-Defaulting Lenders may, to the extent permitted by applicable law, by notice in writing to Borrower and such Person, remove such Person as Agent and, in consultation with Borrower, appoint a successor. If no such successor shall have been so appointed by the non-Defaulting Lenders and shall have accepted such appointment within thirty (30) days (or such earlier day as shall be agreed by the non-Defaulting Lenders) (the "**Removal Effective Date**"), then such removal shall nonetheless become effective in accordance with such notice on the Removal Effective Date.

11 NOTICES

All notices, consents, requests, approvals, demands, or other communication by any party to this Agreement or any other Loan Document must be in writing and shall be deemed to have been validly served, given, or delivered: (a) upon the earlier of actual receipt and three (3) Business Days after deposit in the U.S. mail, first class, registered or certified mail return receipt requested, with proper postage prepaid; (b) upon transmission, when sent by electronic mail or facsimile transmission; (c) one (1) Business Day after deposit with a reputable overnight courier with all charges prepaid; or (d) when delivered, if hand-delivered by messenger, all of which shall be addressed to the party to be notified and sent to the address, facsimile number, or email address indicated below. Agent or Borrower may change its mailing or electronic mail address or facsimile number by giving the other party written notice thereof in accordance with the terms of this Section 11.

If to Borrower: Phasebio Pharmaceuticals, Inc.

1 Great Valley Parkway, Suite 30
Malvern, PA 19355
Attn: Jonathan Mow, CEO
Email: jonathan.mow@phasebio.com

If to Agent or SVB:Silicon Valley Bank

3475 Piedmont Road, Suite 560
Atlanta, GA 30305
Attn: Myron Jensen
Email: MJensen@svb.com

with a copy to:DLA Piper, LLP

401 B Street, Suite 1700
San Diego, CA 92101
Attn: Laurie Hutchins
Fax: 858-638-5041
Email: laurie.hutchins@dlapiper.com

If to WestRiver:WestRiver Innovation Lending Fund VIII, L.P.

c/o WestRiver Management, LLC
3720 Carillon Point
Kirkland, Washington 98033-7455
Attn: Harper Ellison
Email: Harper@wrg.vc

12 CHOICE OF LAW, VENUE AND JURY TRIAL WAIVER

Except as otherwise expressly provided in any of the Loan Documents, California law governs the Loan Documents without regard to principles of conflicts of law. Except to the extent otherwise set forth in the Loan Documents, Borrower, Agent and Lenders each submit to the exclusive jurisdiction of the State and Federal courts in Santa Clara County, California; provided, however, that nothing in this Agreement shall be deemed to operate to preclude Agent or Lenders from bringing suit or taking other legal action in any other jurisdiction to realize on the Collateral or any other security for the Obligations, or to enforce a judgment or other court order in favor of Agent or any Lender. Borrower expressly submits and consents in advance to such jurisdiction in any action or suit commenced in any such court, and Borrower hereby waives any objection that it may have based upon lack of personal jurisdiction, improper venue, or forum non conveniens and hereby consents to the granting of such legal or equitable relief as is deemed appropriate by such court. Borrower hereby waives personal service of the summons, complaints, and other process issued in such action or suit and agrees that service of such summons, complaints, and other process may be made by registered or certified mail addressed to Borrower at the address set forth in, or subsequently provided by Borrower in accordance with, Section 11 of this Agreement and that service so made shall be deemed completed upon the earlier to occur of Borrower's actual receipt thereof or three (3) days after deposit in the U.S. mails, proper postage prepaid.

TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, BORROWER, AGENT AND EACH LENDER EACH WAIVE THEIR RIGHT TO A JURY TRIAL OF ANY CLAIM OR CAUSE OF ACTION ARISING OUT OF OR BASED UPON THIS AGREEMENT, THE LOAN DOCUMENTS OR ANY CONTEMPLATED TRANSACTION, INCLUDING CONTRACT, TORT, BREACH OF DUTY AND ALL OTHER CLAIMS. THIS WAIVER IS A MATERIAL INDUCEMENT FOR ALL PARTIES TO ENTER INTO THIS AGREEMENT. EACH PARTY HAS REVIEWED THIS WAIVER WITH ITS COUNSEL.

WITHOUT INTENDING IN ANY WAY TO LIMIT THE PARTIES' AGREEMENT TO WAIVE THEIR RESPECTIVE RIGHT TO A TRIAL BY JURY, if the above waiver of the right to a trial by jury is not enforceable, the parties hereto agree that any and all disputes or controversies of any nature between them arising at any time shall be decided by a reference to a private judge, mutually selected by the parties (or, if they cannot agree, by the Presiding Judge of the Santa Clara County, California Superior Court) appointed in accordance with California Code of Civil Procedure Section 638 (or pursuant to comparable provisions of federal law if the dispute falls within the exclusive jurisdiction of the federal courts), sitting without a jury, in Santa Clara County, California; and the parties hereby

submit to the jurisdiction of such court. The reference proceedings shall be conducted pursuant to and in accordance with the provisions of California Code of Civil Procedure §§ 638 through 645.1, inclusive. The private judge shall have the power, among others, to grant provisional relief, including without limitation, entering temporary restraining orders, issuing preliminary and permanent injunctions and appointing receivers. All such proceedings shall be closed to the public and confidential and all records relating thereto shall be permanently sealed. If during the course of any dispute, a party desires to seek provisional relief, but a judge has not been appointed at that point pursuant to the judicial reference procedures, then such party may apply to the Santa Clara County, California Superior Court for such relief. The proceeding before the private judge shall be conducted in the same manner as it would be before a court under the rules of evidence applicable to judicial proceedings. The parties shall be entitled to discovery which shall be conducted in the same manner as it would be before a court under the rules of discovery applicable to judicial proceedings. The private judge shall oversee discovery and may enforce all discovery rules and orders applicable to judicial proceedings in the same manner as a trial court judge. The parties agree that the selected or appointed private judge shall have the power to decide all issues in the action or proceeding, whether of fact or of law, and shall report a statement of decision thereon pursuant to California Code of Civil Procedure § 644(a). Nothing in this paragraph shall limit the right of any party at any time to exercise self-help remedies, foreclose against collateral, or obtain provisional remedies. The private judge shall also determine all issues relating to the applicability, interpretation, and enforceability of this paragraph.

This Section 12 shall survive the termination of this Agreement.

13 GENERAL PROVISIONS

13.1 Termination Prior to Maturity Date; Survival. All covenants, representations and warranties made in this Agreement continue in full force until this Agreement has terminated pursuant to its terms and all Obligations have been satisfied. So long as Borrower has satisfied the Obligations (other than inchoate indemnity obligations, any other obligations which, by their terms, are to survive the termination of this Agreement, and any Obligations under Bank Services Agreements that are cash collateralized in accordance with Section 4.1 of this Agreement), this Agreement may be terminated prior to the Growth Capital Maturity Date by Borrower, effective three (3) Business Days after written notice of termination is given to Agent. Those obligations that are expressly specified in this Agreement as surviving this Agreement's termination shall continue to survive notwithstanding this Agreement's termination. No termination of this Agreement shall in any way affect or impair any right or remedy of Agent or any Lender, nor shall any such termination relieve Borrower of any Obligation to any Lender, until all of the Obligations (other than inchoate indemnification obligations) have been paid and performed in full. Those Obligations that are expressly specified in this Agreement as surviving this Agreement's termination shall continue to survive notwithstanding this Agreement's termination and payment in full of the Obligations then outstanding.

13.2 Successors and Assigns. This Agreement binds and is for the benefit of the successors and permitted assigns of each party. Borrower may not assign this Agreement or any rights or obligations under it without Agent and Lenders' prior written consent (which may be granted or withheld in Agent's and Lenders' sole discretion). Agent and each Lender has the right, without the consent of or notice to Borrower, to sell, transfer, assign, negotiate, or grant participation in all or any part of, or any interest in, such Lender's obligations, rights, and benefits under this Agreement and the other Loan Documents (other than the Warrant, as to which assignment, transfer and other such actions are governed by the terms thereof).

13.3 Indemnification. Borrower agrees to indemnify, defend and hold Agent, each Lender and their respective directors, officers, employees, agents, attorneys, or any other Person affiliated with or representing Agent or any Lender (each, an "**Indemnified Person**") harmless against: (i) all obligations, demands, claims, and liabilities (collectively, "**Claims**") claimed or asserted by any other party in connection with the transactions contemplated by the Loan Documents; and (ii) all losses or expenses (including Lenders' Expenses) in any way suffered, incurred, or paid by such Indemnified Person as a result of, following from, consequential to, or arising from transactions between Agent, Lenders and Borrower contemplated by the Loan Documents (including reasonable attorneys' fees and expenses), except for Claims and/or losses directly caused by such Indemnified Person's gross negligence or willful misconduct. This Section 13.3 shall survive until all statutes of limitation with respect to the Claims, losses, and expenses for which indemnity is given shall have run.

13.4 Time of Essence. Time is of the essence for the performance of all Obligations in this Agreement.

13.5 Severability of Provisions. Each provision of this Agreement is severable from every other provision in determining the enforceability of any provision.

13.6 Correction of Loan Documents. Agent may correct patent errors and fill in any blanks in the Loan Documents consistent with the agreement of the parties.

13.7 Amendments in Writing; Waiver; Integration. No purported amendment or modification of any Loan Document, or waiver, discharge or termination of any obligation under any Loan Document, or release, or subordinate Lenders' security interest in, or consent to the transfer of, any Collateral shall be enforceable or admissible unless, and only to the extent, expressly set forth in a writing signed by Agent, with the consent of the Lenders in accordance with the Lender Intercreditor Agreement or, if such item is not addressed in the Lender Intercreditor Agreement, as consented to by a majority of the Lenders, and Borrower. Without limiting the generality of the foregoing, no oral promise or statement, nor any action, inaction, delay, failure to require performance or course of conduct shall operate as, or evidence, an amendment, supplement or waiver or have any other effect on any Loan Document. Any waiver granted shall be limited to the specific circumstance expressly described in it, and shall not apply to any subsequent or other circumstance, whether similar or dissimilar, or give rise to, or evidence, any obligation or commitment to grant any further waiver. The Loan Documents represent the entire agreement about this subject matter and supersede prior negotiations or agreements. All prior agreements, understandings, representations, warranties, and negotiations between the parties about the subject matter of the Loan Documents merge into the Loan Documents. In the event any provision of any other Loan Document is inconsistent with the provisions of this Agreement, the provisions of this Agreement shall exclusively control.

13.8 Counterparts. This Agreement may be executed in any number of counterparts and by different parties on separate counterparts, each of which, when executed and delivered, is an original, and all taken together, constitute one Agreement.

13.9 Confidentiality. Agent and each Lender agrees to maintain the confidentiality of Information (as defined below), except that Information may be disclosed (a) to Agent and/or any Lender's subsidiaries or Affiliates, and their respective employees, directors, investors, potential investors, agents, attorneys, accountants and other professional advisors (collectively, "**Representatives**" and, together with Agent and the Lenders, collectively, "**Lender Entities**"); (b) to prospective transferees, assignees, credit providers or purchasers of any Lender's interests under or in connection with this Agreement and their Representatives (provided, however, Lenders shall use their best efforts to obtain any such prospective transferee's, assignee's, credit provider's, or purchaser's or their Representatives' agreement to the terms of this provision); (c) as required by law, regulation, subpoena, or other order; (d) to Agent's or any Lender's regulators or as otherwise required in connection with Agent's or any Lender's examination or audit; (e) as Agent or any Lender considers appropriate in exercising remedies under the Loan Documents; and (f) to third-party service providers of Agent and/or any Lender so long as such service providers have executed a confidentiality agreement with Agent or the Lenders, as applicable, with terms no less restrictive than those contained herein. The term "**Information**" means all information received from Borrower regarding Borrower or its business, in each case other than information that is either: (i) in the public domain or in Agent's or any Lender's possession when disclosed to Agent or such Lender, or becomes part of the public domain (other than as a result of its disclosure by Agent or a Lender in violation of this Agreement) after disclosure to Agent and/or the Lenders; or (ii) disclosed to Agent and/or a Lender by a third party, if Agent or such Lender, as applicable, does not know that the third party is prohibited from disclosing the information.

Lender Entities may use anonymous forms of confidential information for aggregate datasets, for analyses or reporting, and for any other uses not expressly prohibited in writing by Borrower. The provisions of the immediately preceding sentence shall survive termination of this Agreement.

13.10 Attorneys' Fees, Costs and Expenses. In any action or proceeding between Borrower and any Lender arising out of or relating to the Loan Documents, the prevailing party shall be entitled to recover its reasonable attorneys' fees and other costs and expenses incurred, in addition to any other relief to which it may be entitled.

13.11 Right of Setoff. Borrower hereby grants to Agent, for the ratable benefit of the Lenders, a Lien, security interest, and a right of setoff as security for all Obligations to Agent and the Lenders, whether now existing or hereafter arising upon and against all deposits, credits, collateral and property, now or hereafter in the possession,

custody, safekeeping or control of Agent or any entity under the control of Agent (including a subsidiary of Agent) or in transit to any of them. At any time after the occurrence and during the continuance of an Event of Default, without demand or notice, Agent or any Lender may setoff the same or any part thereof and apply the same to any Obligation of Borrower then due regardless of the adequacy of any other collateral securing the Obligations. ANY AND ALL RIGHTS TO REQUIRE AGENT OR ANY LENDER TO EXERCISE ITS RIGHTS OR REMEDIES WITH RESPECT TO ANY OTHER COLLATERAL WHICH SECURES THE OBLIGATIONS, PRIOR TO EXERCISING ITS RIGHT OF SETOFF WITH RESPECT TO SUCH DEPOSITS, CREDITS OR OTHER PROPERTY OF BORROWER, ARE HEREBY KNOWINGLY, VOLUNTARILY AND IRREVOCABLY WAIVED.

13.12 Electronic Execution of Documents. The words “execution,” “signed,” “signature” and words of like import in any Loan Document shall be deemed to include electronic signatures or the keeping of records in electronic form, each of which shall be of the same legal effect, validity and enforceability as a manually executed signature or the use of a paper-based recordkeeping systems, as the case may be, to the extent and as provided for in any applicable law, including, without limitation, any state law based on the Uniform Electronic Transactions Act.

13.13 Captions. The headings used in this Agreement are for convenience only and shall not affect the interpretation of this Agreement.

13.14 Construction of Agreement. The parties mutually acknowledge that they and their attorneys have participated in the preparation and negotiation of this Agreement. In cases of uncertainty this Agreement shall be construed without regard to which of the parties caused the uncertainty to exist.

13.15 Relationship. The relationship of the parties to this Agreement is determined solely by the provisions of this Agreement. The parties do not intend to create any agency, partnership, joint venture, trust, fiduciary or other relationship with duties or incidents different from those of parties to an arm’s-length contract.

13.16 Third Parties. Nothing in this Agreement, whether express or implied, is intended to: (a) confer any benefits, rights or remedies under or by reason of this Agreement on any persons other than the express parties to it and their respective permitted successors and assigns; (b) relieve or discharge the obligation or liability of any person not an express party to this Agreement; or (c) give any person not an express party to this Agreement any right of subrogation or action against any party to this Agreement.

13.17 Patriot Act. Each Lender hereby notifies Borrower that pursuant to the requirements of the USA PATRIOT Act, it is required to obtain, verify and record information that identifies Borrower and each of its Subsidiaries, which information includes the names and addresses of each Borrower and each of its Subsidiaries and other information that will allow Lender, as applicable, to identify Borrower and each of its Subsidiaries in accordance with the USA PATRIOT Act.

14 DEFINITIONS

14.1 Definitions. As used in the Loan Documents, the word “shall” is mandatory, the word “may” is permissive, the word “or” is not exclusive, the words “includes” and “including” are not limiting, the singular includes the plural, and numbers denoting amounts that are set off in brackets are negative. As used in this Agreement, the following capitalized terms have the following meanings:

“**Account**” is any “account” as defined in the Code or any other applicable law with such additions to such term as may hereafter be made, and includes, without limitation, all accounts receivable and other sums owing to Borrower.

“**Account Debtor**” is any “account debtor” as defined in the Code or any other applicable law with such additions to such term as may hereafter be made.

“**Affiliate**” is, with respect to any Person, each other Person that owns or controls directly or indirectly the Person, any Person that controls or is controlled by or is under common control with the Person, and each of that

Person's senior executive officers, directors, partners and, for any Person that is a limited liability company, that Person's managers and members.

“**Agent**” is defined in the preamble hereof.

“**Agreement**” is defined in the preamble hereof.

“**Amortization Start Date**” is the first day of the first month following the end of the Interest-Only Period.

“**Authorized Signer**” is any individual listed in Borrower's Borrowing Resolution who is authorized to execute the Loan Documents, including any Credit Extension request, on behalf of Borrower.

“**Bank Services**” are any products, credit services, and/or financial accommodations previously, now, or hereafter provided to Borrower or any of its Subsidiaries by SVB or any SVB Affiliate, including, without limitation, any letters of credit, cash management services (including, without limitation, merchant services, direct deposit of payroll, business credit cards, and check cashing services), interest rate swap arrangements, and foreign exchange services as any such products or services may be identified in SVB's various agreements related thereto (each, a “**Bank Services Agreement**”).

“**Bank Services Agreement**” is defined in the definition of Bank Services.

“**Board**” means Borrower's board of directors.

“**Borrower**” is defined in the preamble hereof.

“**Borrower's Books**” are all Borrower's books and records including ledgers, federal and state tax returns, records regarding Borrower's assets or liabilities, the Collateral, business operations or financial condition, and all computer programs or storage or any equipment containing such information.

“**Borrowing Resolutions**” are, with respect to any Person, those resolutions adopted by such Person's board of directors (and, if required under the terms of such Person's Operating Documents, stockholders) and delivered by such Person to Agent approving the Loan Documents to which such Person is a party and the transactions contemplated thereby, together with a certificate executed by its secretary on behalf of such Person certifying (a) such Person has the authority to execute, deliver, and perform its obligations under each of the Loan Documents to which it is a party, (b) that set forth as a part of or attached as an exhibit to such certificate is a true, correct, and complete copy of the resolutions then in full force and effect authorizing and ratifying the execution, delivery, and performance by such Person of the Loan Documents to which it is a party, (c) the name(s) of the Person(s) authorized to execute the Loan Documents, including any Credit Extension request, on behalf of such Person, together with a sample of the true signature(s) of such Person(s), and (d) that Agent and Lenders may conclusively rely on such certificate unless and until such Person shall have delivered to Agent and Lenders a further certificate canceling or amending such prior certificate.

“**Business Day**” is any day that is not a Saturday, Sunday or a day on which Agent is closed.

“**Cash Equivalents**” means (a) marketable direct obligations issued or unconditionally guaranteed by the United States or any agency or any State thereof having maturities of not more than one (1) year from the date of acquisition; (b) commercial paper maturing no more than one (1) year after its creation and having the highest rating from either Standard & Poor's Ratings Group or Moody's Investors Service, Inc.; (c) SVB's certificates of deposit issued maturing no more than one (1) year after issue; and (d) money market funds at least ninety-five percent (95%) of the assets of which constitute Cash Equivalents of the kinds described in clauses (a) through (c) of this definition.

“**Change in Control**” means (a) at any time, any “person” or “group” (as such terms are used in Sections 13(d) and 14(d) of the Exchange Act), shall become, or obtain rights (whether by means of warrants, options or otherwise) to become, the “beneficial owner” (as defined in Rules 13(d)-3 and 13(d)-5 under the Exchange Act), directly or indirectly, of forty percent (40.0%) or more of the ordinary voting power for the election of directors of

Borrower (determined on a fully diluted basis) other than by the sale of Borrower's equity securities in a public offering or to venture capital or private equity investors so long as Borrower identifies to the Agent and the Lenders the venture capital or private equity investors at least seven (7) Business Days prior to the closing of the transaction and provides to Agent and the Lenders a description of the material terms of the transaction; (b) during any period of twelve (12) consecutive months, a majority of the members of the board of directors or other equivalent governing body of Borrower cease to be composed of individuals (i) who were members of that board or equivalent governing body on the first day of such period, (ii) whose election or nomination to that board or equivalent governing body was approved by individuals referred to in clause (i) above constituting at the time of such election or nomination at least a majority of that board or equivalent governing body or (iii) whose election or nomination to that board or other equivalent governing body was approved by individuals referred to in clauses (i) and (ii) above constituting at the time of such election or nomination at least a majority of that board or equivalent governing body; or (c) at any time, Borrower shall cease to own and control, of record and beneficially, directly or indirectly, one hundred percent (100.0%) of each class of outstanding capital stock of each Subsidiary of Borrower free and clear of all Liens (except Liens created by this Agreement).

"Claims" is defined in Section 13.3.

"Code" is the Uniform Commercial Code, as the same may, from time to time, be enacted and in effect in the State of California; provided, that, to the extent that the Code is used to define any term herein or in any Loan Document and such term is defined differently in different Articles or Divisions of the Code, the definition of such term contained in Article or Division 9 shall govern; provided further, that in the event that, by reason of mandatory provisions of law, any or all of the attachment, perfection, or priority of, or remedies with respect to, Agent's Lien on any Collateral is governed by the Uniform Commercial Code in effect in a jurisdiction other than the State of California, the term **"Code"** shall mean the Uniform Commercial Code as enacted and in effect in such other jurisdiction solely for purposes of the provisions thereof relating to such attachment, perfection, priority, or remedies and for purposes of definitions relating to such provisions.

"Collateral" is any and all properties, rights and assets of Borrower described on Exhibit A attached hereto.

"Collateral Account" is any Deposit Account, Securities Account, or Commodity Account.

"Commitment" and **"Commitments"** means the Growth Capital Commitment(s).

"Commodity Account" is any "commodity account" as defined in the Code or any other applicable law with such additions to such term as may hereafter be made.

"Compliance Certificate" is that certain certificate in the form attached hereto as Exhibit B.

"Contingent Obligation" is, for any Person, any direct or indirect liability, contingent or not, of that Person for (a) any indebtedness, lease, dividend, letter of credit or other obligation of another such as an obligation, in each case, directly or indirectly guaranteed, endorsed, co-made, discounted or sold with recourse by that Person, or for which that Person is directly or indirectly liable; (b) any obligations for undrawn letters of credit for the account of that Person; and (c) all obligations from any interest rate, currency or commodity swap agreement, interest rate cap or collar agreement, or other agreement or arrangement designated to protect a Person against fluctuation in interest rates, currency exchange rates or commodity prices; but "Contingent Obligation" does not include endorsements in the ordinary course of business. The amount of a Contingent Obligation is the stated or determined amount of the primary obligation for which the Contingent Obligation is made or, if not determinable, the maximum reasonably anticipated liability for it determined by the Person in good faith; but the amount may not exceed the maximum of the obligations under any guarantee or other support arrangement.

"Control Agreement" is any control agreement entered into among the depository institution at which Borrower maintains a Deposit Account or the securities intermediary or commodity intermediary at which Borrower maintains a Securities Account or a Commodity Account, Borrower, and Agent pursuant to which Agent obtains control (within the meaning of the Code or any other applicable law) for the benefit of the Lenders over such Deposit Account, Securities Account, or Commodity Account.

“**Copyrights**” are any and all copyright rights, copyright applications, copyright registrations and like protections in each work of authorship and derivative work thereof, whether published or unpublished and whether or not the same also constitutes a trade secret.

“**Credit Extension**” is any Growth Capital Advance or any other extension of credit by any Lender for Borrower’s benefit.

“**Default Rate**” is defined in Section 2.2(b).

“**Defaulting Lender**” is, subject to Section 10.10(b), any Lender that (a) has failed to (i) fund all or any portion of its Growth Capital Advances within two (2) Business Days of the date such Growth Capital Advances were required to be funded hereunder unless such Lender notifies Agent and Borrower in writing that such failure is the result of such Lender’s reasonable determination that one or more conditions precedent to funding (each of which conditions precedent, together with any applicable default, shall be specifically identified in such writing) has not been satisfied, or (ii) pay to Agent or any other Lender any other amount required to be paid by it hereunder within two (2) Business Days of the date when due, (b) has notified Borrower or Agent in writing that it does not intend to comply with its funding obligations hereunder, or has made a public statement to that effect (unless such writing or public statement relates to such Lender’s obligation to fund a Growth Capital Advance hereunder and states that such position is based on such Lender’s reasonable determination that a condition precedent to funding (which condition precedent, together with any applicable default, shall be specifically identified in such writing or public statement) cannot be satisfied), (c) has failed, within three (3) Business Days after written request by Agent or Borrower, to confirm in writing to Agent and Borrower that it will comply with its prospective funding obligations hereunder (provided that such Lender shall cease to be a Defaulting Lender pursuant to this clause (c) upon receipt of such written confirmation by Agent and Borrower), or (d) has, or has a direct or indirect parent company that has, (i) become the subject of an Insolvency Proceeding, or (ii) had appointed for it a receiver, custodian, conservator, trustee, administrator, assignee for the benefit of creditors or similar Person charged with reorganization or liquidation of its business or assets, including the Federal Deposit Insurance Corporation or any other state or federal regulatory authority acting in such a capacity; provided that a Lender shall not be a Defaulting Lender solely by virtue of the ownership or acquisition of any equity interest in that Lender or any direct or indirect parent company thereof by a Governmental Authority so long as such ownership interest does not result in or provide such Lender with immunity from the jurisdiction of courts within the United States or from the enforcement of judgments or writs of attachment on its assets or permit such Lender (or such Governmental Authority) to reject, repudiate, disavow or disaffirm any contracts or agreements made with such Lender. Any determination by Agent that a Lender is a Defaulting Lender under any one or more of clauses (a) through (d) above shall be conclusive and binding absent manifest error, and such Lender shall be deemed to be a Defaulting Lender (subject to Section 10.10(b)) upon delivery of written notice of such determination to Borrower and each Lender.

“**Deposit Account**” is any “deposit account” as defined in the Code with such additions to such term as may hereafter be made.

“**Designated Deposit Account**” is the multicurrency account denominated in Dollars, account number XXXXXXXX254, maintained by Borrower with SVB (provided, however, if no such account number is included, then the Designated Deposit Account shall be any deposit account of Borrower maintained with SVB as chosen by the Lenders).

“**Disbursement Letter**” is that certain form attached hereto as Exhibit E.

“**Dollars**,” “**dollars**” or use of the sign “\$” means only lawful money of the United States and not any other currency, regardless of whether that currency uses the “\$” sign to denote its currency or may be readily converted into lawful money of the United States.

“**Dollar Equivalent**” is, at any time, (a) with respect to any amount denominated in Dollars, such amount, and (b) with respect to any amount denominated in a Foreign Currency, the equivalent amount therefor in Dollars as determined by Agent at such time on the basis of the then-prevailing rate of exchange in San Francisco, California, for sales of the Foreign Currency for transfer to the country issuing such Foreign Currency.

“**Effective Date**” is defined in the preamble hereof.

“**Equipment**” is all “equipment” as defined in the Code or any other applicable law with such additions to such term as may hereafter be made, and includes without limitation all machinery, fixtures, goods, vehicles (including motor vehicles and trailers), and any interest in any of the foregoing.

“**ERISA**” is the Employee Retirement Income Security Act of 1974, and its regulations.

“**Event of Default**” is defined in Section 8.

“**Exchange Act**” is the Securities Exchange Act of 1934, as amended.

“**Federal Funds Effective Rate**” means, for any day, the weighted average of the rates on overnight federal funds transactions with members of the Federal Reserve System arranged by federal funds brokers, as published on the next succeeding Business Day by the Federal Reserve Bank of New York, or, if such rate is not so published for any day that is a Business Day, the average of the quotations for the day of such transactions received by SVB from three federal funds brokers of recognized standing selected by it.

“**Final Payment**” is a payment (in addition to and not in substitution for the regular monthly payments of principal plus accrued interest) equal to the original principal amount of each Growth Capital Advance extended by the Lenders to Borrower hereunder multiplied by six percent (6.0%), due on the earliest to occur of (a) the Growth Capital Maturity Date, (b) the payment in full of such Growth Capital Advance, (c) as required by Section 2.1.1(d) or 2.1.1(e) or (d) the termination of this Agreement.

“**Foreign Currency**” means lawful money of a country other than the United States.

“**Funding Date**” is any date on which a Credit Extension is made to or for the account of Borrower which shall be a Business Day.

“**FX Contract**” is any foreign exchange contract by and between Borrower and SVB under which Borrower commits to purchase from or sell to SVB a specific amount of Foreign Currency on a specified date.

“**GAAP**” is generally accepted accounting principles set forth in the opinions and pronouncements of the Accounting Principles Board of the American Institute of Certified Public Accountants and statements and pronouncements of the Financial Accounting Standards Board or in such other statements by such other Person as may be approved by a significant segment of the accounting profession, which are applicable to the circumstances as of the date of determination.

“**General Intangibles**” is all “general intangibles” as defined in the Code or any other applicable law in effect on the date hereof with such additions to such term as may hereafter be made, and includes without limitation, all Intellectual Property, claims, income and other tax refunds, security and other deposits, payment intangibles, contract rights, options to purchase or sell real or personal property, rights in all litigation presently or hereafter pending (whether in contract, tort or otherwise), insurance policies (including without limitation key man, property damage, and business interruption insurance), payments of insurance and rights to payment of any kind.

“**Governmental Approval**” is any consent, authorization, approval, order, license, franchise, permit, certificate, accreditation, registration, filing or notice, of, issued by, from or to, or other act by or in respect of, any Governmental Authority.

“**Governmental Authority**” is any nation or government, any state or other political subdivision thereof, any agency, authority, instrumentality, regulatory body, court, central bank or other entity exercising executive, legislative, judicial, taxing, regulatory or administrative functions of or pertaining to government, any securities exchange and any self-regulatory organization.

“**Group Member**” means Borrower and its Subsidiaries.

“**Growth Capital Advance**” and “**Growth Capital Advances**” are defined in Section 2.1.1(a).

“**Growth Capital Commitment**” means, for any Lender, the obligation of such Lender to make a Growth Capital Advance as and when available, up to the principal amount shown on Schedule 1.1. “**Growth Capital Commitments**” means the aggregate amount of such commitments of all Lenders.

“**Growth Capital Loan Commitment Percentage**” means, as to any Lender at any time, the percentage (carried out to the fourth decimal place) of the Growth Capital Commitments represented by such Lender’s Growth Capital Commitment at such time. The initial Growth Capital Commitment Percentage of each Lender is set forth opposite the name of such Lender on Schedule 1.1.

“**Growth Capital Line**” is a Growth Capital Advance or Growth Capital Advances in an aggregate principal amount of up to Fifteen Million Dollars (\$15,000,000).

“**Growth Capital Maturity Date**” means March 1, 2023.

“**Indebtedness**” is (a) indebtedness for borrowed money or the deferred price of property or services, such as reimbursement and other obligations for surety bonds and letters of credit, (b) obligations evidenced by notes, bonds, debentures or similar instruments, (c) capital lease obligations, and (d) Contingent Obligations.

“**Indemnified Person**” is defined in Section 13.3.

“**Information**” is defined in Section 13.9.

“**Insolvency Proceeding**” is any proceeding by or against any Person under the United States Bankruptcy Code or any other bankruptcy or insolvency law, including assignments for the benefit of creditors, compositions, extensions generally with its creditors, or proceedings seeking reorganization, arrangement, or other relief.

“**Intellectual Property**” means, with respect to any Person, all of such Person’s right, title, and interest in and to the following:

- (a) its Copyrights, Trademarks and Patents;
- (b) any and all trade secrets and trade secret rights, including, without limitation, any rights to unpatented inventions, know-how and operating manuals;
- (c) any and all source code;
- (d) any and all design rights which may be available to such Person;
- (e) any and all claims for damages by way of past, present and future infringement of any of the foregoing, with the right, but not the obligation, to sue for and collect such damages for said use or infringement of the Intellectual Property rights identified above; and
- (f) all amendments, renewals and extensions of any of the Copyrights, Trademarks or Patents.

“**Interest-Only Period**” is the period of time from the Effective Date through December 31, 2019; provided, however, if Borrower achieves the Tranche C Milestone, the Interest-Only Period shall automatically, and with no further action required by the parties hereto, be extended to June 30, 2020.

“**Inventory**” is all “inventory” as defined in the Code or any other applicable law in effect on the date hereof with such additions to such term as may hereafter be made, and includes without limitation all merchandise, raw materials, parts, supplies, packing and shipping materials, work in process and finished products, including without limitation such inventory as is temporarily out of Borrower’s custody or possession or in transit and including any returned goods and any documents of title representing any of the above.

“**Investment**” is any beneficial ownership interest in any Person (including stock, partnership interest or other securities), and any loan, advance or capital contribution to any Person.

“**Key Person**” is each of Borrower’s (a) Chief Executive Officer, who is Jonathan Mow as of the Effective Date, (b) Chief Financial Officer, who is John Sharp as of the Effective Date, and (c) Chief Medical Officer, who is John Lee as of the Effective Date.

“**Lender**” and “**Lenders**” is defined in the preamble.

“**Lender Entities**” is defined in Section 13.9.

“**Lender Intercreditor Agreement**” is, collectively, any and all intercreditor agreement, master arrangement agreement or similar agreement by and between WestRiver and SVB, as each may be amended from time to time in accordance with the provisions thereof.

“**Lenders’ Expenses**” are all of Agent’s and the Lenders’ audit fees and expenses, costs, and expenses (including reasonable attorneys’ fees and expenses) for preparing, amending, negotiating, administering, defending and enforcing the Loan Documents (including, without limitation, those incurred in connection with appeals or Insolvency Proceedings) or otherwise incurred with respect to Borrower.

“**Letter of Credit**” is a standby or commercial letter of credit issued by SVB upon request of Borrower based upon an application, guarantee, indemnity, or similar agreement.

“**Lien**” is a claim, mortgage, deed of trust, levy, charge, pledge, security interest or other encumbrance of any kind, whether voluntarily incurred or arising by operation of law or otherwise against any property.

“**Loan Documents**” are, collectively, this Agreement and any schedules, exhibits, certificates, notices, and any other documents related to this Agreement, the Warrants, the Perfection Certificate, each Disbursement Letter, the Lender Intercreditor Agreement, any Bank Services Agreement, any Control Agreement, any subordination agreement, any note, or notes or guaranties executed by Borrower, and any other present or future agreement by Borrower with or for the benefit of Agent and the Lenders in connection with this Agreement or Bank Services, all as amended, restated, or otherwise modified.

“**Material Adverse Change**” is: (a) a material impairment in the perfection or priority of Agent’s, for the ratable benefit of the Lenders, Lien in the Collateral or in the value of such Collateral; (b) a material adverse change in the business, operations, or condition (financial or otherwise) of Borrower; or (c) a material impairment of the prospect of repayment of any portion of the Obligations.

“**Monthly Financial Statements**” is defined in Section 6.2(a).

“**Obligations**” are Borrower’s obligations to pay when due any debts, principal, interest, fees, Lenders’ Expenses, the Final Payment, the Prepayment Premium, and other amounts Borrower owes Agent or any Lender now or later, whether under this Agreement, the other Loan Documents (other than the Warrant), or otherwise, including, without limitation, all obligations relating to Bank Services, if any, and including interest accruing after Insolvency Proceedings begin and debts, liabilities, or obligations of Borrower assigned to Agent and/or the Lenders, and to perform Borrower’s duties under the Loan Documents (other than the Warrant).

“**Operating Documents**” are, for any Person, such Person’s formation documents, as certified by the Secretary of State (or equivalent agency) of such Person’s jurisdiction of organization on a date that is no earlier than thirty (30) days prior to the Effective Date, and, (a) if such Person is a corporation, its bylaws in current form, (b) if such Person is a limited liability company, its limited liability company agreement (or similar agreement), and (c) if such Person is a partnership, its partnership agreement (or similar agreement), each of the foregoing with all current amendments or modifications thereto.

“**Patents**” means all patents, patent applications and like protections including without limitation improvements, divisions, continuations, renewals, reissues, extensions and continuations-in-part of the same.

“**Payment/Advance Form**” is that certain form attached hereto as Exhibit C.

“**Payment Date**” is the first (1st) calendar day of each month.

“**Perfection Certificate**” is defined in Section 5.1.

“**Permitted Indebtedness**” is:

- (a) Borrower’s Indebtedness to Agent and the Lenders under this Agreement and the other Loan Documents;
- (b) Indebtedness existing on the Effective Date which is shown on the Perfection Certificate;
- (c) Subordinated Debt;
- (d) unsecured Indebtedness to trade creditors incurred in the ordinary course of business;
- (e) Indebtedness incurred as a result of endorsing negotiable instruments received in the ordinary course of business;
- (f) Indebtedness secured by Liens permitted under clauses (a) and (c) of the definition of “Permitted Liens” hereunder;

(g) extensions, refinancings, modifications, amendments and restatements of any items of Permitted Indebtedness (a) through (f) above; provided that the principal amount thereof is not increased or the terms thereof are not modified to impose more burdensome terms upon Borrower or its Subsidiary, as the case may be.

“**Permitted Investments**” are:

- (a) Investments (including, without limitation, Subsidiaries) existing on the Effective Date which are shown on the Perfection Certificate;
- (b) Investments consisting of Cash Equivalents;
- (c) Investments consisting of the endorsement of negotiable instruments for deposit or collection or similar transactions in the ordinary course of Borrower;
- (d) Investments accepted in connection with Transfers permitted by Section 7.1;

(e) Investments consisting of the creation of a Subsidiary for the purpose of consummating a merger transaction permitted by Section 7.3 of this Agreement, which is otherwise a Permitted Investment;

(f) Investments (i) by Borrower in Subsidiaries not to exceed Fifty Thousand Dollars (\$50,000.00) in the aggregate in any fiscal year and (ii) by Subsidiaries in other Subsidiaries not to exceed Fifty Thousand Dollars (\$50,000.00) in the aggregate in any fiscal year or in Borrower;

(g) Investments consisting of (i) travel advances and employee relocation loans and other employee loans and advances in the ordinary course of business, and (ii) loans to employees, officers or directors relating to the purchase of equity securities of Borrower or its Subsidiaries pursuant to employee stock purchase plans or agreements approved by Borrower’s Board of Directors;

(h) Investments (including debt obligations) received in connection with the bankruptcy or reorganization of customers or suppliers and in settlement of delinquent obligations of, and other disputes with, customers or suppliers arising in the ordinary course of business; and

(i) Investments consisting of notes receivable of, or prepaid royalties and other credit extensions, to customers and suppliers who are not Affiliates, in the ordinary course of business; provided that this paragraph (i) shall not apply to Investments of Borrower in any Subsidiary.

“Permitted Liens” are:

(a) Liens existing on the Effective Date which are shown on the Perfection Certificate or arising under this Agreement and the other Loan Documents;

(b) Liens for taxes, fees, assessments or other government charges or levies, either (i) not due and payable or (ii) being contested in good faith and for which Borrower maintains adequate reserves on its Books, provided that no notice of any such Lien has been filed or recorded under the Internal Revenue Code of 1986, as amended, and the Treasury Regulations adopted thereunder;

(c) purchase money Liens (i) on Equipment acquired or held by Borrower incurred for financing the acquisition of the Equipment securing no more than Two Hundred Fifty Thousand Dollars (\$250,000.00) in the aggregate amount outstanding, or (ii) existing on Equipment when acquired, if the Lien is confined to the property and improvements and the proceeds of the Equipment;

(d) Liens of carriers, warehousemen, suppliers, or other Persons that are possessory in nature arising in the ordinary course of business so long as such Liens attach only to Inventory, securing liabilities in the aggregate amount not to exceed Two Hundred Fifty Thousand Dollars (\$250,000.00), and which are not delinquent or remain payable without penalty or which are being contested in good faith and by appropriate proceedings which proceedings have the effect of preventing the forfeiture or sale of the property subject thereto;

(e) Liens arising from attachments or judgments, orders, or decrees in circumstances not constituting an Event of Default under Sections 8.4 and 8.7; and

(f) Liens incurred in the extension, renewal or refinancing of the indebtedness secured by Liens described in (a) through (d), but any extension, renewal or replacement Lien must be limited to the property encumbered by the existing Lien and the principal amount of the indebtedness may not increase.

“Person” is any individual, sole proprietorship, partnership, limited liability company, joint venture, company, trust, unincorporated organization, association, corporation, institution, public benefit corporation, firm, joint stock company, estate, entity or government agency.

“Prepayment Premium” shall be an additional fee, payable to Agent, for the ratable benefit of the Lenders based on their Pro Rata Share, with respect to the Growth Capital Advances, in an amount equal to:

(a) for a prepayment of the Growth Capital Advances made on or prior to the first (1st) anniversary of the Effective Date, three percent (3.0%) of the then outstanding principal amount of the Growth Capital Advances immediately prior to the date of such prepayment;

(b) for a prepayment of the Growth Capital Advances made after the first (1st) anniversary of the Effective Date, but on or prior to the second (2nd) anniversary of the Effective Date, two percent (2.0%) of the then outstanding principal amount of the Growth Capital Advances immediately prior to the date of such prepayment; and

(c) for a prepayment of the Growth Capital Advances made after the second (2nd) anniversary of the Effective Date, but prior to the Growth Capital Maturity Date, one percent (1.0%) of the then outstanding principal amount of the Growth Capital Advances immediately prior to the date of such prepayment.

“Prime Rate” is the rate of interest per annum from time to time published in the money rates section of The Wall Street Journal or any successor publication thereto as the “prime rate” then in effect; provided that, in the event

such rate of interest is less than zero, such rate shall be deemed to be zero for purposes of this Agreement; and provided further that if such rate of interest, as set forth from time to time in the money rates section of The Wall Street Journal, becomes unavailable for any reason as determined by Agent, the “Prime Rate” shall mean the rate of interest per annum announced by SVB as its prime rate in effect at its principal office in the State of California (such SVB announced Prime Rate not being intended to be the lowest rate of interest charged by SVB in connection with extensions of credit to debtors); provided that, in the event such rate of interest is less than zero, such rate shall be deemed to be zero for purposes of this Agreement.

“**Pro Rata Share**” is, as of any date of determination, with respect to each Lender, a percentage (expressed as a decimal, rounded to the ninth decimal place) determined by *dividing* the outstanding principal amount of Growth Capital Advances held by such Lender by the aggregate outstanding principal amount of all Growth Capital Advances.

“**Registered Organization**” is any “registered organization” as defined in the Code or any other applicable law with such additions to such term as may hereafter be made.

“**Removal Effective Date**” is defined in Section 10.10(d).

“**Repayment Schedule**” means the period of time equal to thirty-nine (39) consecutive months; provided, however, upon the occurrence of the Tranche C Milestone, the Repayment Schedule shall mean the period of time equal to thirty-three (33) consecutive months.

“**Representatives**” is defined in Section 13.9.

“**Requirement of Law**” is as to any Person, the organizational or governing documents of such Person, and any law (statutory or common), treaty, rule or regulation or determination of an arbitrator or a court or other Governmental Authority, in each case applicable to or binding upon such Person or any of its property or to which such Person or any of its property is subject.

“**Responsible Officer**” is any of the Chief Executive Officer, President and Chief Financial Officer of Borrower.

“**Restricted License**” is any material license or other agreement with respect to which Borrower is the licensee (a) that prohibits or otherwise restricts Borrower from granting a security interest in, or a fixed or floating charge over, Borrower’s interest in such license or agreement or any other property, or (b) for which a default under or termination of could interfere with the Agent’s right to sell any Collateral.

“**SEC**” shall mean the Securities and Exchange Commission, any successor thereto, and any analogous Governmental Authority.

“**Securities Account**” is any “securities account” as defined in the Code or any other applicable law with such additions to such term as may hereafter be made.

“**Subordinated Debt**” is indebtedness incurred by Borrower subordinated to all of Borrower’s now or hereafter indebtedness to Agent and the Lenders (pursuant to a subordination, intercreditor, or other similar agreement in form and substance satisfactory to Agent and the Lenders, entered into between Agent, the Lenders and the other creditor), on terms acceptable to Agent and the Lenders.

“**Subsidiary**” is, as to any Person, a corporation, partnership, limited liability company or other entity of which shares of stock or other ownership interests having ordinary voting power (other than stock or such other ownership interests having such power only by reason of the happening of a contingency) to elect a majority of the board of directors or other managers of such corporation, partnership or other entity are at the time owned, or the management of which is otherwise controlled, directly or indirectly through one or more intermediaries, or both, by such Person. Unless the context otherwise requires, each reference to a Subsidiary herein shall be a reference to a Subsidiary of Borrower.

“**SVB**” is defined in the preamble hereof.

“**SVB Loan Agreement**” means that certain Loan and Security Agreement dated as of October 18, 2017 between Borrower and Bank as amended, modified, supplemented and/or restated from time to time.

“**Trademarks**” means any trademark and servicemark rights, whether registered or not, applications to register and registrations of the same and like protections, and the entire goodwill of the business of Borrower connected with and symbolized by such trademarks.

“**Tranche A**” is defined in Section 2.1.1(a) hereof.

“**Tranche A Growth Capital Advance**” is defined in Section 2.1.1(a).

“**Tranche B**” is defined in Section 2.1.1(a) hereof.

“**Tranche B Draw Period**” is the period of time from the Effective Date through May 31, 2019.

“**Tranche B Growth Capital Advance**” is defined in Section 2.1.1(a).

“**Tranche C**” is defined in Section 2.1.1(a) hereof.

“**Tranche C Growth Capital Advance**” is defined in Section 2.1.1(a).

“**Tranche C Milestone**” means (i) Borrower has requested and the Lenders have made the Tranche B Growth Capital Advance to Borrower, and (ii) Borrower delivers to the Lenders evidence, in form and substance satisfactory to the Lenders in their sole discretion, confirming that Borrower has received FDA clearance to initiate its Phase 3 clinical trial for PB2452.

“**Transfer**” is defined in Section 7.1.

“**Warrant**” means, collectively, (i) that certain Warrant to Purchase Stock dated as of October 18, 2017 issued by Borrower in favor of SVB, (ii) that certain Warrant to Purchase Stock dated as of the Effective Date issued by Borrower in favor of SVB, (iii) that certain Warrant to Purchase Stock dated as of the Effective Date issued by Borrower in favor of WestRiver and (iv) any other warrant to purchase stock issued by Borrower to SVB or WestRiver heretofore or hereafter, in each case as may be amended, modified, supplemented and/or restated from time to time.

“**WestRiver**” is defined in the preamble hereof.

[Signature page follows.]

IN WITNESS WHEREOF, the parties hereto have caused this Agreement to be executed as of the Effective Date.

BORROWER:

PHASEBIO PHARMACEUTICALS, INC.

By /s/ Jonathan P. Mow
Name: Jonathan P. Mow
Title: CEO

AGENT:

SILICON VALLEY BANK, as Agent

By /s/ Myron O. Jensen
Name: Myron O. Jensen
Title: Vice President

LENDERS:

SILICON VALLEY BANK, as Lender

By /s/ Myron O. Jensen
Name: Myron O. Jensen
Title: Vice President

WESTRIVER INNOVATION LENDING FUND VIII, L.P, as Lender

By /s/ Trent Dawson
Name: Trent Dawson
Title: Chief Financial Officer

[Signature Page to Loan and Security Agreement]

SCHEDULE 1.1

LENDERS AND GROWTH CAPITAL COMMITMENTS

<u>Lender</u>	<u>Tranche A Loan Advance Commitment</u>	<u>Tranche A Loan Advance Commitment</u>
		<u>Percentage</u>
Silicon Valley Bank	\$3,750,000.00	50.0000%
WestRiver Innovation Lending Fund VIII, L.P.	\$3,750,000.00	50.0000%
<u>TOTAL</u>	<u>\$7,500,000.00</u>	<u>100.0000%</u>

<u>Lender</u>	<u>Tranche B Loan Advance Commitment</u>	<u>Tranche B Loan Advance Commitment</u>
		<u>Percentage</u>
Silicon Valley Bank	\$1,250,000.00	50.0000%
WestRiver Innovation Lending Fund VIII, L.P.	\$1,250,000.00	50.0000%
<u>TOTAL</u>	<u>\$2,500,000.00</u>	<u>100.0000%</u>

<u>Lender</u>	<u>Tranche C Loan Advance Commitment</u>	<u>Tranche C Loan Advance Commitment</u>
		<u>Percentage</u>
Silicon Valley Bank	\$2,500,000.00	50.0000%
WestRiver Innovation Lending Fund VIII, L.P.	\$2,500,000.00	50.0000%
<u>TOTAL</u>	<u>\$5,000,000.00</u>	<u>100.0000%</u>

EXHIBIT A

The Collateral consists of all of Borrower's right, title and interest in and to the following personal property:

All goods, Accounts (including health-care receivables), Equipment, Inventory, contract rights or rights to payment of money, leases, license agreements, franchise agreements, General Intangibles (except as provided below), commercial tort claims, documents, instruments (including any promissory notes), chattel paper (whether tangible or electronic), cash, deposit accounts, certificates of deposit, fixtures, letters of credit rights (whether or not the letter of credit is evidenced by a writing), securities, and all other investment property, supporting obligations, and financial assets, whether now owned or hereafter acquired, wherever located; and

all Borrower's Books relating to the foregoing, and any and all claims, rights and interests in any of the above and all substitutions for, additions, attachments, accessories, accessions and improvements to and replacements, products, proceeds and insurance proceeds of any or all of the foregoing.

Notwithstanding the foregoing, the Collateral does not include any Intellectual Property; provided, however, the Collateral shall include all Accounts and all proceeds of Intellectual Property. If a judicial authority (including a U.S. Bankruptcy Court) would hold that a security interest in the underlying Intellectual Property is necessary to have a security interest in such Accounts and such property that are proceeds of Intellectual Property, then the Collateral shall automatically, and effective as of the Effective Date, include the Intellectual Property to the extent necessary to permit perfection of Agent's, for the ratable benefit of the Lenders, security interest in such Accounts and such other property of Borrower that are proceeds of the Intellectual Property.

Pursuant to the terms of a certain negative pledge arrangement with Agent and the Lenders, Borrower has agreed not to encumber any of its Intellectual Property without Agent and the Lenders' prior written consent.

EXHIBIT B

COMPLIANCE CERTIFICATE

TO: SILICON VALLEY BANK, as Agent, SVB and WESTRIVER as Lenders
FROM: PHASEBIO PHARMACEUTICALS, INC., a Delaware corporation
DATE: _____

The undersigned authorized officer of PHASEBIO PHARMACEUTICALS, INC. ("**Borrower**") certifies that under the terms and conditions of the Loan and Security Agreement among Borrower, SVB, and WestRiver (as amended, the "**Loan Agreement**"), (1) Borrower is in complete compliance for the period ending _____ with all required covenants except as noted below, (2) there are no Events of Default, (3) all representations and warranties in the Agreement are true and correct in all material respects on this date except as noted below; provided, however, that such materiality qualifier shall not be applicable to any representations and warranties that already are qualified or modified by materiality in the text thereof; and provided, further that those representations and warranties expressly referring to a specific date shall be true, accurate and complete in all material respects as of such date, (4) Borrower, and each of its Subsidiaries, has timely filed all required tax returns and reports, and Borrower has timely paid all foreign, federal, state and local taxes, assessments, deposits and contributions owed by Borrower except as otherwise permitted pursuant to the terms of Section 5.8 of the Agreement, and (5) no Liens have been levied or claims made against Borrower or any of its Subsidiaries relating to unpaid employee payroll or benefits of which Borrower has not previously provided written notification to Agent. Attached are the required documents supporting the certification. The undersigned certifies that these are prepared in accordance with GAAP consistently applied from one period to the next except as explained in an accompanying letter or footnotes. The undersigned acknowledges that no borrowings may be requested at any time or date of determination that Borrower is not in compliance with any of the terms of the Agreement, and that compliance is determined not just at the date this certificate is delivered. Capitalized terms used but not otherwise defined herein shall have the meanings given them in the Agreement.

Please indicate compliance status by circling Yes/No under "**Complies**" column.

<u>Reporting Covenants</u>	<u>Required</u>	<u>Complies</u>
Monthly financial statements with Compliance Certificate	Monthly within 30 days	Yes No
Annual financial statement (CPA Audited)	FYE within 150 days	Yes No
10-Q, 10-K and 8-K	Within 5 days after filing with SEC	Yes No
Board Projections	At least annually and within 60 days of FYE, and as amended/updated by Board approval	Yes No

Other Matters

Have there been any amendments of or other changes to the capitalization table of Borrower and to the Operating Documents of Borrower or any of its Subsidiaries? If yes, provide copies of any such amendments or changes with this Compliance Certificate. Yes No

The following are the exceptions with respect to the certification above: (If no exceptions exist, state "No exceptions to note.")

PHASEBIO PHARMACEUTICALS, INC.

By: _____
Name: _____
Title: _____

SVB USE ONLY

Received by: _____
AUTHORIZED SIGNER

Date: _____

Verified: _____
AUTHORIZED SIGNER

Date: _____

Compliance Status: Yes No

EXHIBIT C

LOAN PAYMENT/ADVANCE REQUEST FORM

Fax To:

Date: _____

LOAN PAYMENT: PHASEBIO PHARMACEUTICALS, INC.

From Account # _____ To Account # _____
 (Deposit Account #) (Loan Account #)

Principal \$ _____ and/or Interest \$ _____

Authorized Signature: _____ Phone Number: _____
 Print Name/Title: _____

LOAN ADVANCE:

Complete *Outgoing Wire Request* section below if all or a portion of the funds from this loan advance are for an outgoing wire.

From Account # _____ To Account # _____
 (Loan Account #) (Deposit Account #)

Amount of Growth Capital Advance \$ _____

All Borrower's representations and warranties in the Loan and Security Agreement are true, correct and complete on the date of the request for an advance:

Authorized Signature: _____ Phone Number: _____
 Print Name/Title: _____

OUTGOING WIRE REQUEST:

Complete only if all or a portion of funds from the loan advance above is to be wired.

Deadline for same day processing is noon, Eastern Time

Beneficiary Name: _____ Amount of Wire: \$ _____
 Beneficiary Bank: _____ Account Number: _____
 City and State: _____

Beneficiary Bank Transit (ABA) #: _____ Beneficiary Bank Code (Swift, Sort, Chip, etc.): _____
(For International Wire Only)

Intermediary Bank: _____ Transit (ABA) #: _____
 For Further Credit to: _____

Special Instruction: _____

By signing below, I (we) acknowledge and agree that my (our) funds transfer request shall be processed in accordance with and subject to the terms and conditions set forth in the agreements(s) covering funds transfer service(s), which agreements(s) were previously received and executed by me (us).

Authorized Signature: _____ 2nd Signature (if required): _____
 Print Name/Title: _____ Print Name/Title: _____
 Telephone #: _____ Telephone #: _____

EXHIBIT D

BORROWING RESOLUTIONS



CORPORATE BORROWING CERTIFICATE

BORROWER: PHASEBIO PHARMACEUTICALS, INC.
LENDERS: SILICON VALLEY BANK ("Bank") and WESTRIVER INNOVATION LENDING FUND VIII, L.P.

DATE: March 25, 2019

I hereby certify as follows, as of the date set forth above:

- I am the Secretary, Assistant Secretary or other officer of Borrower. My title is as set forth below.
- Borrower's exact legal name is set forth above. Borrower is a corporation existing under the laws of the State of Delaware.
- Attached hereto are true, correct and complete copies of Borrower's Certificate of Incorporation (including amendments), as filed with the Secretary of State of the state in which Borrower is incorporated as set forth above. Such Certificate of Incorporation have not been amended, annulled, rescinded, revoked or supplemented, and remain in full force and effect as of the date hereof.
- The following resolutions were duly and validly adopted by Borrower's Board of Directors at a duly held meeting of such directors (or pursuant to a unanimous written consent or other authorized corporate action). Such resolutions are in full force and effect as of the date hereof and have not been in any way modified, repealed, rescinded, amended or revoked, and the Lenders may rely on them until the Lenders receive written notice of revocation from Borrower.

RESOLVED, that **any one** of the following officers or employees of Borrower, whose names, titles and signatures are below, may act on behalf of Borrower:

<u>Name</u>	<u>Title</u>	<u>Signature</u>	<u>Authorized to Add or Remove Signatories</u>
_____	_____	_____	<input type="checkbox"/>
_____	_____	_____	<input type="checkbox"/>
_____	_____	_____	<input type="checkbox"/>
_____	_____	_____	<input type="checkbox"/>

RESOLVED FURTHER, that **any one** of the persons designated above with a checked box beside his or her name may, from time to time, add or remove any individuals to and from the above list of persons authorized to act on behalf of Borrower.

RESOLVED FURTHER, that such individuals may, on behalf of Borrower:

Borrow Money. Borrow money from Lenders.

Execute Loan Documents. Execute any loan documents the Lenders require.

Grant Security. Grant the Lenders a security interest in any of Borrower's assets.

Negotiate Items. Negotiate or discount all drafts, trade acceptances, promissory notes, or other indebtedness in which Borrower has an interest and receive cash or otherwise use the proceeds.

Apply for Letters of Credit. Apply for letters of credit from Bank.

Enter Derivative Transactions. Execute spot or forward foreign exchange contracts, interest rate swap agreements, or other derivative transactions with Bank.

Issue Warrants. Issue warrants for Borrower's capital stock.

Further Acts. Designate other individuals to request advances, pay fees and costs and execute other documents or agreements (including documents or agreement that waive Borrower's right to a jury trial) they believe to be necessary to effect these resolutions.

RESOLVED FURTHER, that all acts authorized by the above resolutions and any prior acts relating thereto are ratified.

5. The persons listed above are Borrower's officers or employees with their titles and signatures shown next to their names.

PHASEBIO PHARMACEUTICALS, INC.

By: _____

Name: _____

Title: _____

**** If the Secretary, Assistant Secretary or other certifying officer executing above is designated by the resolutions set forth in paragraph 4 as one of the authorized signing officers, this Certificate must also be signed by a second authorized officer or director of Borrower.*

I, the _____ of Borrower, hereby certify as to paragraphs 1 through 5 above, as of the date set forth above.

By: _____

Name: _____

Title: _____

EXHIBIT E

Form of Disbursement Letter

[see attached]

DISBURSEMENT LETTER

[DATE]

The undersigned, being the duly elected and acting _____ of **PHASEBIO PHARMACEUTICALS, INC.**, a Delaware corporation ("**Borrower**") does hereby certify to (a) **SILICON VALLEY BANK**, a California corporation ("**SVB**"), in its capacity as administrative agent and collateral agent ("**Agent**"), (b) **SILICON VALLEY BANK**, a California corporation, as a lender, (c) **WESTRIVER INNOVATION LENDING FUND VIII, L.P.**, a Delaware limited partnership ("**WestRiver**"), as a lender (SVB and WestRiver and each of the other "**Lenders**" from time to time a party hereto are referred to herein collectively as the "**Lenders**" and each individually as a "**Lender**") in connection with that certain Loan and Security Agreement dated as of March 25, 2019, by and among Borrower, Agent and the Lenders from time to time party thereto (the "**Loan Agreement**"; with other capitalized terms used below having the meanings ascribed thereto in the Loan Agreement) that:

1. The representations and warranties made by Borrower in Section 5 of the Loan Agreement and in the other Loan Documents are true and correct in all material respects as of the date hereof.
2. No event or condition has occurred that would constitute an Event of Default under the Loan Agreement or any other Loan Document.
3. Borrower is in compliance with the covenants and requirements contained in Sections 4, 6 and 7 of the Loan Agreement.
4. All conditions referred to in Section 3 of the Loan Agreement to the making of a Credit Extension to be made on or about the date hereof have been satisfied or waived by Agent.
5. No Material Adverse Change has occurred.
6. The undersigned is an Authorized Signer.

[Balance of Page Intentionally Left Blank]

7. The proceeds of the Growth Capital Advance shall be disbursed as follows:

Disbursement from SVB:		
Loan Amount		\$ _____
Plus:		
--Deposit Received		\$ _____
Less:		
--Agent's Legal Fees		\$ (_____)
Net Proceeds due from SVB:		\$ _____
Disbursement from WestRiver:		
Loan Amount		\$ _____
Plus:		
--Deposit Received		\$ _____
Less:		
--Lender's Legal Fees		\$ (_____)
Net Proceeds due from WestRiver:		\$ _____
TOTAL GROWTH CAPITAL ADVANCE NET PROCEEDS FROM LENDERS		\$ _____

8. The aggregate net proceeds of the Growth Capital Advance shall be transferred to the Designated Deposit Account as follows:

Account Name:	Phasebio Pharmaceuticals, Inc.
Bank Name:	Silicon Valley Bank
Bank Address:	3003 Tasman Drive Santa Clara, California 95054
Account Number:	_____
ABA Number:	_____

[Balance of Page Intentionally Left Blank]

Dated as of the date first set forth above.

BORROWER:

PHASEBIO PHARMACEUTICALS, INC.

By _____
Name: _____
Title: _____

AGENT AND LENDER:

SILICON VALLEY BANK

By _____
Name: _____
Title: _____

LENDER:

SILICON VALLEY BANK

By _____
Name: _____
Title: _____

LENDER:

WESTRIVER INNOVATION LENDING FUND
VIII, L.P.

By _____
Name: _____
Title: _____

[Signature Page to Disbursement Letter]

ANNEX I

Form of Warrant

[see attached]

Marketing Consent Form

SVB Financial Group is proud of our business relationships and occasionally likes to promote these relationships. We would like to use your company’s information and logo for promotional and marketing purposes in SVB Financial Group member businesses (collectively “SVB”) materials. While we would appreciate your consent to all of the uses listed below, please review and select all of the uses that you consent to below.

Approved Use(s)

Indicate your selection(s) by checking the boxes below

- Marketing:** You consent to SVB’s use of Company’s name, logo and images provided to us in written and oral presentations, advertising, marketing and PR materials, professional lists and websites.
- Deal Terms:** You consent to SVB’s inclusion of the size and type of any loan or credit facility alongside your company’s name in any oral presentations, advertising, marketing and PR materials, customer lists, and websites.
- Reference:** You consent to SVB’s use of Company and representatives’ names as a reference for SVB.
- Testimonial:** You consent to SVB’s use of Company and representatives’ names and quotations in written and oral presentations, marketing and PR materials, and websites. Our practice is to send you a draft of any quotation concerning Company prior to publishing.
- News release:** You consent to SVB’s use of Company’s name, trademarks, service marks, quotations and images provided to us in the SVB’s news releases concerning Company. Our practice is to send you a draft of any news release concerning Company prior to publishing.

Logos

In order to maintain the integrity of your logos, please provide them in:

- ▶ Full color and black and white versions, with or without taglines
- ▶ At least 300 dpi in PNG, EPS, TIF, or JPG formats (please do not send PDF or website logos).

Names

Please make sure to print the Company name, and any individual names and titles as you would like them displayed in materials or lists.

Company name	PHASEBIO PHARMACEUTICALS, INC.
Additional names	

You grant to SVB a limited license to use the information for the limited purposes above, which you can revoke upon written notice to SVB. The signer below acknowledges that he or she has authority to bind the Company to this consent. SVB will not be responsible for versions that were printed prior to receiving notice revoking any such consent. Company is solely responsible for defense and maintenance of its intellectual property.

Please contact your Relationship Advisor or SVB representative if you have any questions.

Accepted or Agreed on Behalf Of Company or Yourself

Name		Title	
Signature		Today’s date	MARCH 25, 2019
Address			
Phone number		Email	

Return this completed form and any attachments to your Relationship Advisor or SVB via email at logo@svb.com.

CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY [*], HAS BEEN OMITTED BECAUSE IT IS NOT MATERIAL AND WOULD LIKELY CAUSE COMPETITIVE HARM TO THE COMPANY IF PUBLICLY DISCLOSED.**

MASTER SERVICES AGREEMENT

This Master Services Agreement (the "**Agreement**") is entered into as of November 14, 2018 (the "**Effective Date**") by and between PhaseBio Pharmaceuticals, Inc., a Delaware corporation having a place of business at 1 Great Valley Parkway, Suite 30, Malvern, Pennsylvania 19355 ("**PhaseBio**") and BioVectra Inc., a company registered under the laws of the province of Prince Edward Island, Canada having a place of business at 11 Aviation Avenue, Charlottetown, PE, C1 E0A1, Canada ("**Contractor**"). PhaseBio and Contractor may be referred to herein individually as a "**Party**" and collectively as the "**Parties**."

WHEREAS, contractor has expertise manufacturing and assembly of products similar to the product (as defined below); and

WHEREAS, the parties contemplate that PhaseBio will purchase from contractor, and contractor will manufacture and supply to PhaseBio the products as phase bio may order from time to time pursuant to the terms and conditions set forth in a separate supply agreement ("**Supply Agreement**") to be negotiated by the parties in good faith; and

WHEREAS, in preparation for such the manufacture and supply of the products pursuant to the supply agreement, the parties desire to conduct certain activities and have contractor perform certain services pursuant to the terms and conditions set forth herein.

NOW, THEREFORE, in consideration of the foregoing, and for other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the parties agree as follows:

1. DEFINITIONS. As used in this Agreement:

1.1 "Adverse Event" shall mean any adverse event associated with the use of any Product in humans, whether or not considered drug-related, including an adverse event occurring in the course of the use of a Product in professional practice, in studies, in investigations or in tests or an adverse event occurring from Product overdose (whether accidental or intentional), from Product abuse, or from Product withdrawal, as well as any toxicity, sensitivity, failure of expected pharmacological action, or laboratory abnormality that is, or is thought by the reporter to be, serious or associated with relevant clinical signs or symptoms.

1.2 "Applicable Laws" means all relevant federal, state and local laws, statutes, rules, and regulations that are applicable to a Party's activities hereunder.

1.3 "Confidentiality Agreement" means that certain Confidential Disclosure Agreement by and between the Parties dated as of May 14, 2018.

1.4 "Contractor Background Technology" shall mean all Information that Contractor uses in the manufacture of, or performance of manufacturing and development services with respect to, biological products on behalf of its clients, that is either: (a) owned or controlled by Contractor on the Effective Date (other than as a result of PhaseBio disclosing or providing the same to Contractor); or (b) developed or acquired, and owned or controlled, by Contractor during the Term independently of any activities conducted pursuant to this Agreement.

1.5 "Contractor Improvement" shall mean any improvement to the Contractor Background Technology that: (a) is made solely by Contractor in the course of performing Services; (b) is not specific to the manufacture of Product; and (c) does not use or incorporate any Product, Materials, or Confidential Information of PhaseBio.

1.6 "Contractor Technology" shall mean Contractor Background Technology and Contractor Improvements.

1.7 "Deliverables" means the items to be provided or actually provided by Contractor to PhaseBio under this Agreement, including items specifically designated or characterized as deliverables in a Statement of Work.

1.8 "Developments" means ideas, inventions, improvements, novel techniques, original works of authorship, discoveries, developments, know-how, trade secrets, patents, patent applications, copyrights, trademarks, studies, cost and pricing data, customer lists, technologies, methods, processes, formulas, research, methods, procedures, designs, models, testing systems, algorithms, computer software and programs (including source and object code and related documentation), data and results, reports, notes, memoranda, laboratory notebooks, drawings, technical information and materials; in each case, whether or not patentable or copyrightable; that, in each case, are made, generated, developed, conceived, or first reduced to practice by Contractor, whether solely or jointly with PhaseBio, either (i) in the course of performance of the Services hereunder or (ii) using any Confidential Information disclosed or made available by or on behalf of the PhaseBio to Contractor or to which Contractor obtains access in connection with the activities contemplated by this Agreement. Without limiting the generality of the foregoing, Developments include all Product Improvements.

1.9 "FDA" means the United States Food and Drug Administration or any successor entity thereto.

1.10 "Governmental Authority" means any national, international, federal, state, provincial or local government, or political subdivision thereof, or any multinational organization or any authority, agency or commission entitled to exercise any administrative, executive, judicial, legislative, police, regulatory or taxing authority or power, any court or tribunal (or any department, bureau or division thereof, or any governmental arbitrator or arbitral body).

1.11 "Information" means any and all technical information and know-how, including without limitation, data, instructions, processes, formulae, trade secrets, expert opinions and other information (in written or other tangible form) including, without limitation, any biological, chemical, pharmacological, toxicological, clinical, assay, control and manufacturing data, biological materials, manufacturing or related technology, analytical methodology, chemical and quality control procedures, protocols, techniques, improvements and results of experimentation and testing.

1.12 "Intellectual Property" means ideas, concepts, discoveries, inventions, developments, know-how, trade secrets, techniques, methodologies, modifications, innovations, improvements, writings, documentation, electronic code, data and rights (whether or not protectable under state, federal or foreign patent, trademark, copyright or similar laws) or the like, whether or not written or otherwise fixed in any form or medium, regardless of the media on which contained and whether or not patentable or copyrightable.

1.13 "Materials" means those materials supplied by PhaseBio for use in connection with the Services.

1.14 "PhaseBio Contact" means the PhaseBio contact person for a particular Statement of Work as identified in such Statement of Work.

1.15 "Product Improvements" means any invention, discovery, development or modification with respect to any Product or relating to the development, manufacture, use or commercialization of any Product, whether or not patented or patentable, including any enhancement in the efficiency, operation, manufacture, ingredients, preparation, presentation, formulation, means of delivery or dosage of any Product, any discovery or development of any new or expanded methods of treatment, use or indications for any Product or any discovery or development that improves the stability, safety or efficacy of any Product; in each case that is conceived, discovered, developed or otherwise made by Contractor, whether solely or jointly with PhaseBio, under or in connection with this Agreement or the performance of the Services hereunder.

1.16 "Product" means PhaseBio's drug candidate known as PB2452 ("**PB2452**").

1.17 "Regulatory Approval" means all approvals, including pricing approvals, that are necessary for the commercial sale of a Licensed Product in a given country or regulatory jurisdiction.

1.18 "Regulatory Authority" means any applicable Governmental Authority responsible for granting regulatory approvals for Product, including the FDA and the EMA, and any corresponding national or regional regulatory authorities.

1.19 "Services" means the services related to any Product specifically set forth in a Statement of Work.

1.20 "Specifications" means any procedures, process parameters, analytical tests and other attributes and written specifications for the Services and Deliverables included in a Statement of Work.

1.21 "Work Product" shall mean any and all data and results and products (interim and final) of the Services performed by Contractor, whether tangible or intangible, including all inventions, discoveries, developments, innovations, methods, techniques, protocols, processes, procedures, specifications, trade secrets, know-how, modifications, enhancements, improvements, substances, materials, writings and documentation (whether or not protectable under patent, trademark, copyright or other intellectual property laws), that are made, developed, perfected, designed, conceived or first reduced to practice by Contractor's employees, agents, consultants, subcontractors or other representatives, either solely or jointly with employees, agents, consultants or other representatives of PhaseBio, in the course and as a result of performing the Services; but excluding Contractor Technology.

2. SERVICES

2.1 Statements of Work. From time to time, PhaseBio may submit to Contractor written work orders substantially in the form of Exhibit A that specify the Services to be performed and any Deliverables to be provided by Contractor under such work orders, as well as the terms and conditions (including Specifications (if applicable), delivery and performance schedules, and fees) under which Contractor shall perform such Services. Upon acceptance of a work order by Contractor (in writing or by performance as set forth below), such work order becomes a "**Statement of Work.**" If Contractor begins to perform services under a work order, Contractor shall be deemed to have accepted such work order in the form submitted by PhaseBio. Contractor may not perform any services on behalf of PhaseBio other than pursuant to a Statement of Work established as set forth above. In the event of any conflict between this Agreement and a Statement of Work, this Agreement shall control unless the Statement of Work expressly refers to the Parties' intent to alter the terms of this Agreement with respect to that Statement of Work. For clarity, PhaseBio may retain third parties other than Contractor to provide services similar or identical to the Services provided under this Agreement.

2.2 Performance of Services. Contractor shall perform the Services in accordance with the terms of this Agreement, the applicable Statement of Work, and all Applicable Laws. Contractor shall provide, at its own expense, a place of work (unless the Statement of Work requires Contractor to perform the Services on PhaseBio's premises), and all equipment, tools, and other materials necessary to complete the Statement of Work.

2.3 Change Proposals. Upon the receipt of a proposal from PhaseBio to change the terms of a Statement of Work (a "**Change Proposal**"), Contractor shall promptly provide to PhaseBio (a) any information requested in such proposal, and (b) its written acceptance or rejection of the proposal. Contractor may reject any Change Proposal that materially shortens the delivery or performance schedule or materially alters the Services or Deliverables, and may not unreasonably reject any other Change Proposal. If Contractor begins to adhere to a Change Proposal or does not reject the Change Proposal in writing within five (5) days after its receipt thereof, Contractor shall be deemed to have accepted such Change Proposal. PhaseBio's submission or Contractor's reasonable rejection (in accordance with this Section 2.3) of a Change

Proposal does not constitute a breach of this Agreement. A Change Proposal may, but need not, include an increase in fees payable under the Statement of Work.

2.4 Project Manager. Contractor shall appoint one of its employees as the "**Project Manager**" for each Statement of Work. The Project Manager shall be responsible for all aspects of the Services under such Statement of Work through completion of such Services. The Project Manager shall regularly report progress on such Statement of Work to the PhaseBio Contact for such Statement of Work, and coordinate with such PhaseBio Contact for the performance of the Services. Unless otherwise agreed, all communications between PhaseBio and Contractor regarding the conduct of the Services pursuant to a Statement of Work shall be addressed between such Project Manager and PhaseBio Contact. The Project Manager shall use best efforts to respond to any communication from PhaseBio within [***] after receipt of such communication.

2.5 Timelines. Contractor shall use reasonable efforts to comply with any timelines, milestones, schedules, or target dates for completing the Services or any portion thereof as set forth in a Statement of Work. If at any time Contractor anticipates a delay in meeting such timelines for a Statement of Work, Contractor shall promptly notify PhaseBio in writing of such anticipated delay and the estimated duration of such delay.

2.6 Records. Contractor shall maintain, in good scientific manner, complete and accurate books and records pertaining to Services provided hereunder, in sufficient detail to verify compliance with its obligations under this Agreement. Such books and records shall (a) be appropriate for patent and regulatory purposes, (b) be in compliance with Applicable Law, (c) properly reflect all work done and results achieved in the performance of the Services hereunder, and (d) be retained by Contractor for such period as may be required by Applicable Law. At any time upon PhaseBio's written request, PhaseBio shall have the right, during normal business hours and upon reasonable notice, to inspect and copy any or all such books and records pursuant to this Section 2.6; provided that PhaseBio shall maintain such records and information disclosed therein in accordance with Article 4.

2.7 Additional Agreements. Contractor shall ensure that each of its employees who will have access to any Confidential Information or perform any Services has entered into a binding written agreement that protects PhaseBio's rights and interests to at least the same degree as Sections 2.10, 2.11, 5, 6, 7 and 8 of this Agreement.

2.8 Subcontracting. Contractor may not subcontract or otherwise delegate any of its obligations under this Agreement without PhaseBio's prior written consent on a case-by-case basis for each specific subcontractor proposed by Contractor for a specific task. After receipt of PhaseBio's consent but before allowing a subcontractor to begin performing a task, Contractor shall enter into a written agreement with such subcontractor that obligates such subcontractor (and its personnel involved in the performance of such task) to be bound by the terms and conditions of this Agreement (including the Statement of Work(s) applicable to the task to be performed by such subcontractor), in the same manner as such terms and conditions apply to Contractor. Contractor shall direct and coordinate the services of each subcontractor, and shall ensure the subcontractor's compliance with the terms and conditions of this Agreement. Contractor shall directly retain any approved subcontractor and no contractual relationship shall be created between PhaseBio and subcontractors, other than PhaseBio's position as a third-party beneficiary of the services of

subcontractors and to the written agreements between Contractor and the subcontractors as set forth above. Contractor shall pay a subcontractor using the payment submitted by PhaseBio as part of the overall budget set forth in the Statement of Work. PhaseBio has no obligation to pay any subcontractor. PhaseBio's consent to a subcontractor shall not in any way relieve Contractor of any duty or responsibility under this Agreement. As between PhaseBio and Contractor, Contractor shall perform all Services hereunder, regardless of whether any portion of such Services is delegated pursuant to this Section 2.8.

2.9 Employees. Subject to Section 2.8, Contractor shall conduct the Services solely through its employees and not through any consultants, temporary workers, agents or the like. PhaseBio may, with reasonable justification, refuse or limit Contractor's use of any employee or require Contractor to remove any employee already engaged in the performance of the Services. PhaseBio's exercise of such right shall in no way be construed as relieving Contractor from its obligations under this Agreement.

2.10 Access to PhaseBio Premises. If the Services or any portion thereof are to be performed by Contractor on PhaseBio's premises, PhaseBio shall grant reasonable access to its premises to the employees of Contractor solely to the extent necessary for the performance of such Services and solely for the purpose of permitting such employees to perform such Services. To expedite security processing, Contractor shall give at least twenty-four (24)-hours' prior notice to the applicable PhaseBio Contact prior to Contractor's initial entry onto PhaseBio's premises, informing such PhaseBio Contact the timing of such proposed entry and the names of Contractor's employees to be processed. At the time of initial entry, the employees specified in the preceding sentence shall report to the location directed by PhaseBio for security processing. PhaseBio shall issue appropriate identification badges and access cards that will give such employees entry to PhaseBio's premises for the performance of the Services. Any such badges and cards remain the property of PhaseBio. Contractor shall promptly report any missing badges to PhaseBio, and Contractor shall return the badges to PhaseBio upon completion of the Services to be performed on PhaseBio's premises. Contractor shall instruct such employees to wear the badges in plain sight at all times while working within the limits of PhaseBio's premises. Contractor shall ensure that such employees comply with all instructions given by PhaseBio employees or security personnel, and any other access or other restrictions that may be imposed by PhaseBio.

2.11 Materials. To the extent specified in a particular Statement of Work, PhaseBio shall provide Contractor with sufficient amounts of the Materials for Contractor to perform the Services. PhaseBio retains all right, title, and interest in and to the Materials. Contractor shall use the Materials solely to perform the Services under such Statement of Work and shall comply with PhaseBio's instructions and Applicable Laws. Contractor may not sell, transfer, disclose, or otherwise provide access to the Materials to any person, other than Contractor employee's, or entity without the prior written consent of PhaseBio, and Contractor may not reverse engineer or otherwise attempt to determine the structure, composition, or individual components of the Materials. Promptly upon completion of the applicable Services or earlier upon PhaseBio's request, Contractor shall, according to PhaseBio's instructions, return the Materials to PhaseBio or destroy the Materials and certify such destruction in writing.

2.12 Reports. Upon completion of all Services under a Statement of Work, or at such other times as set forth in the applicable Statement of Work, Contractor shall provide PhaseBio with a written report summarizing all Project Records and Services completed for such Statement

of Work, in both electronic and hard copy. All such reports shall be deemed Confidential Information of PhaseBio.

3. INDEPENDENT CONTRACTOR RELATIONSHIP. Contractor's relation to PhaseBio under this Agreement is that of an independent contractor. Nothing in this Agreement is intended or should be construed to create a partnership, joint venture, or employer-employee relationship between PhaseBio and any of Contractor's employees or agents. Contractor is not the agent of PhaseBio and is not authorized, and may not represent to any third party that it is authorized, to make any commitment or otherwise act on behalf of PhaseBio. Without limiting the generality of the foregoing:

3.1 Benefits and Contributions. Neither Contractor nor any of its employees or agents is entitled to or eligible for any benefits that PhaseBio may make available to its employees, such as group insurance, profit-sharing, or retirement benefits. Because Contractor is an independent contractor, PhaseBio will not withhold or make payments for social security, make unemployment insurance or disability insurance contributions, or obtain workers' compensation insurance on behalf of Contractor or any of its employees or agents.

3.2 Taxes. Contractor is solely responsible for filing all tax returns and submitting all payments as required by any federal, state, local, or foreign tax authority arising from the payment of fees to Contractor under this Agreement, and shall do so in a timely manner. If applicable, PhaseBio shall report the fees paid to Contractor under this Agreement by filing Form 1099-MISC with the Internal Revenue Service as required by law.

4. COMPENSATION

4.1 Fees. Subject to the terms and conditions of this Agreement, PhaseBio shall pay Contractor the fees specified in each Statement of Work ("**Fees**") as Contractor's sole and complete compensation for all Services, Deliverables, and Intellectual Property rights provided by Contractor under such Statement of Work and this Agreement. Contractor shall provide PhaseBio with written, itemized invoices in accordance with the payment schedule set forth in the applicable Statement of Work, with each such invoice specifying the Services performed for which payment is being requested. In no event shall the total amount invoiced under a particular Statement of Work exceed the budget set forth in such Statement of Work, unless as amended by an executed Change Proposal. Contractor may not submit for payment any invoice for services that PhaseBio has not consented to pursuant to an executed Statement of Work or Change Proposal. In no event shall PhaseBio be liable for fees or expenses incurred by Contractor in connection with any services or other work performed by Contractor without PhaseBio's prior written consent.

4.2 Expenses. Unless expressly provided otherwise in the applicable Statement of Work, PhaseBio shall reimburse Contractor for any reasonable expenses for travel undertaken at PhaseBio's request, and other out-of-pocket expenses previously approved by PhaseBio, that are incurred by Contractor or any of its employees in performing the Services (the "**Expenses**"), on the condition that: (a) Contractor provides PhaseBio with invoices for such Expenses and adequate supporting documentation for such invoices; and (b) Contractor complies with PhaseBio's travel policy for the submission and verification of such expenses. Contractor is responsible for obtaining the then-current version of such policy before submitting any invoice for reimbursement.

4.3 Release and Delivery of Product. Where Services involve manufacturing of Product, Contractor is responsible for release of Product to PhaseBio. Contractor shall release Product against the Specifications and shall provide PhaseBio with a Certificate of Analysis, Certificate of Origin and a Certificate of Compliance.

4.4 Delivery of Product. Contractor shall deliver Product to PhaseBio FCA, Charlottetown, PE (INCOTERMS 2010). Contractor shall arrange for the shipment of Product including insurance, customs and clearance to a designated delivery location specified by PhaseBio, at PhaseBio's expense. Contractor shall provide documents for export and support the inspection and export process. Unless requested in writing, Contractor shall deliver Product upon release. PhaseBio will be responsible for any costs related to the storage, handling and insurance fees incurred with respect to storage of Product after release and transfer of ownership.

4.5 Title and Risk of Loss. Title to and risk of loss of or damage to the Product sold hereunder shall pass to PhaseBio upon release of Product. PhaseBio shall assume the risk of loss of or damage to the Product after release, except to the extent that such loss or damage results from the negligence or willful misconduct of Contractor or its representatives, for which Contractor shall retain the risk of loss of or damage to Product.

4.6 Payments. Unless otherwise expressly provided in the applicable Statement of Work payment to Contractor of undisputed Fees and Expenses shall be due [***] following PhaseBio's receipt of the invoice for such Fees and Expenses submitted by Contractor pursuant to Section 4.1 or 4.2 above. Payments shall be addressed to:

BioVectra Inc.
11 Aviation Avenue
Charlottetown, PE
C1E OA1, Canada
Attention: Accounting Department

4.7 Acceptance of Services. PhaseBio may accept or reject the Service or Deliverable, or any portion thereof, in writing within [***] from receipt thereof. Such acceptance or rejection shall be consistent with the criteria set forth in the Statement of Work, if any. If PhaseBio does not reject in writing within [***], the Service or Deliverable shall be considered accepted by PhaseBio. PhaseBio shall clearly state in writing the reasons for any rejection. Where Contractor agrees with assessment of rejection, within [***] of any notice of rejection, Contractor shall present a corrective plan of action to PhaseBio. Upon approval by PhaseBio of the corrective plan, Contractor, at no additional expense to PhaseBio, shall then make the corrections and, where applicable, Contractor shall resubmit the corrected Service or Deliverable to PhaseBio.

4.8 Independent Laboratory Testing. If PhaseBio and Contractor are unable to agree as to whether any Product conforms to the Specifications or warranties, the Parties shall cooperate to have the Product in dispute analyzed by an independent testing laboratory of recognized repute or a mutually acceptable independent GMP consultant in the case of an alleged failure to comply with GMP selected by Contractor and approved by PhaseBio, which approval shall not be unreasonably withheld, conditioned or delayed. The results of such laboratory testing or GMP consultant shall be final and binding on the Parties on the issue of conformance of the Product to the Specifications. If the Product is determined to so conform, then PhaseBio shall bear the cost of the independent laboratory testing or GMP review and pay for the Product in accordance with this Agreement. If the Product is determined not to conform, then Contractor shall bear the cost of the independent laboratory testing or GMP review, and Contractor shall, at PhaseBio's sole discretion, within [***] of the date of such determination, either replace the rejected Product at no cost to Company or promptly refund to PhaseBio the price paid for such Product.

4.9 Disputed Amounts. For disputed invoices or the disputed portion of an invoice, PhaseBio shall use reasonable efforts to provide to Contractor, in writing, within [***], a description of the disputed amounts. PhaseBio and Contractor shall negotiate in a timely, good faith manner to resolve billing queries.

5. AUDITS

5.1 Audit. Contractor shall maintain accurate and complete records and accounts relating to Services provided hereunder, and, in accordance with generally-accepted accounting principles, complete and accurate records of expenses incurred sufficient to document the Fees and Expenses invoiced to PhaseBio for at least three (3) years following the date of the invoice. ("**Records and Accounts**"). Upon request by PhaseBio provided with reasonable prior notice, Contractor shall allow PhaseBio or PhaseBio's authorized representatives to visit Contractor's facilities during normal business hours to observe and verify Contractor's compliance with this Agreement, review the Records and Accounts, inspect those facilities of Contractor which are being utilized in the Services, and to make copies of relevant records. Records and Accounts shall be maintained for a period of three (3) years after the creation of the applicable Record or Account. To assure the quality of Contractor's performance of the Services hereunder, PhaseBio may perform such audits no more than two (2) times in any twelve (12) months; provided, however, PhaseBio may also visit Contractor's offices with reasonable frequency during normal business hours to discuss the progress of the Services. If said audits exceed two (2) times in any twelve (12) month period, PhaseBio shall reimburse Contractor for costs and expenses actually incurred by Contractor in connection with the additional audits, provided, however, that if PhaseBio discovers that Contractor has been overcharging PhaseBio as a result of such audit, Contractor shall refund the amount of any overcharging that is not disputed in good faith by Contractor. In addition, if the amount of any such undisputed overcharge exceeds 10% of the amounts actually due during the period being audited, Contractor shall reimburse PhaseBio for the costs of any said additional audit. All Records and Accounts shall be deemed Confidential Information under the Confidentiality Agreement.

5.2 Monitoring. Contractor shall cooperate with any requests by PhaseBio to monitor the Services to verify that the Services are being performed in accordance with this Agreement and in a timely and satisfactory manner. Contractor shall use its best efforts to facilitate any such monitoring, including providing access to Contractor's employees, agents, equipment, and facilities.

6. REGULATORY.

6.1 Cooperation and Assistance. Contractor shall cooperate with any pre-approval or other type of regulatory inspection by any Regulatory Authority. Without limiting the generality of the foregoing, Contractor shall cooperate with PhaseBio and PhaseBio's representatives in the performance of mock pre-approval inspections in preparation for a pre-approval inspection by a Regulatory Authority in connection with any application for Regulatory Approval of Product. Contractor shall promptly address any findings that are discovered during any such mock pre-approval inspection in advance of any pre-approval inspection by a Regulatory Authority. During the Term, Contractor shall provide all reasonable support and cooperation to PhaseBio in connection with its submissions to Regulatory Authorities in applications for Regulatory Approval or for the purpose of obtaining or maintaining Regulatory Approvals or pre-approval regulatory submissions. Upon PhaseBio's written request, Contractor shall provide to PhaseBio all information, documentation and data, including CMC data, in Contractor's or its permitted subcontractors' possession relating to Product or its manufacture (or true and complete copies thereof) as PhaseBio may require for any purpose, including submissions to Regulatory Authorities in applications for Regulatory Approval or for the purpose of obtaining or maintaining Regulatory Approvals or pre-approval regulatory submissions; in each case, at PhaseBio's expense for actual out-of-pocket costs. In addition, upon PhaseBio's request, Contractor shall review manufacturing-related portions of PhaseBio's draft regulatory submissions for accuracy and conformance with current practice at Contractor, and shall respond to PhaseBio in writing within [***] of such request.

6.2 Adverse Event Reporting. PhaseBio shall be responsible for all reporting to regulatory authorities of Adverse Events associated with the use of any Product supplied by Contractor hereunder. If Contractor becomes aware of any Adverse Events associated with the use of such Products, it shall report all information in its possession regarding such event to PhaseBio within [***] of becoming aware of such information, and shall cooperate with PhaseBio as necessary to report such event to regulatory authorities.

6.3 Regulatory Compliance. Contractor shall comply with all regulatory requirements with respect to Products imposed by applicable laws, rules and regulations upon Contractor as the manufacturer of the Products. Contractor shall, on a timely basis, provide PhaseBio with information in Contractor's possession relevant to its role as the manufacturer of Products that is reasonably necessary for PhaseBio to obtain or maintain Regulatory Approvals or otherwise to comply with applicable regulatory requirements. Contractor shall not file any drug master file ("DMF") for a Product with any Regulatory Authority, except with the prior written consent of PhaseBio. Should any Statement of Work provide for Contractor to develop and file a DMF for a Product, such DMF shall be subject to review, comment and approval by PhaseBio prior to filing. In the event of filing of any DMF for a Product, Contractor shall provide PhaseBio with letters of access to such DMF.

6.4 Cooperation. Contractor will provide to PhaseBio such documentation, data and other information relating to Products as PhaseBio may require for submission to regulatory authorities. Contractor shall also provide, upon request by PhaseBio, information concerning its production processes and quality control procedures with respect to Products.

6.5 Regulatory Inspections. Contractor shall inform PhaseBio within [***] of notification of any regulatory inquiry, communication, or inspection relating to any Product. If Contractor receives any correspondence from any regulatory or governmental agency relating to a Product (including any Form FDA-483 notice, and any FDA refusal to file, rejection or warning letter, even if they do not specifically mention PhaseBio), or any notice of inspection or an inspection visit by any Regulatory Authority that involves a Product or could impact Contractor's ability to produce a Product, Contractor shall notify PhaseBio, and shall deliver to PhaseBio a copy of any such correspondence or notice (if any), within [***] of notification by such Regulatory Authority. Contractor shall permit PhaseBio to, at PhaseBio's option, have PhaseBio's representatives present at any such inspection by a Regulatory Authority. If there are written observations (or any other written communication) by a Regulatory Authority that involve Product or could impact Contractor's ability to produce Product, or any proposed written response by Contractor to any such inspection, Contractor shall inform PhaseBio within [***] and provide PhaseBio with copies of all documentation within [***], and shall have a reasonable opportunity to review and comment on the proposed response.

6.6 Incidents or Accidents. Contractor shall immediately notify PhaseBio in writing of any incident or accident experienced by Contractor that Contractor believes may affect the quality of the Product or Deliverables that Contractor is obligated to deliver hereunder or its ability to meet delivery date obligations hereunder. Contractor shall promptly investigate such incident or accident and shall provide a written report within [***] of the results of the investigation of such incidence or accident to PhaseBio.

7. INTELLECTUAL PROPERTY

7.1 PhaseBio Intellectual Property. PhaseBio shall retain all right, title and interest in and to all Intellectual Property and know-how owned by PhaseBio prior to the Effective Date or made or acquired by PhaseBio during the Term.

7.2 Contractor Intellectual Property. Subject to the licenses set forth in Section 7.4, Contractor shall retain all right, title and interest in and to all Contractor Background Technology.

7.3 Project Intellectual Property. PhaseBio owns all right, title and interest in and to the Developments, Deliverables, and all intellectual property rights and know-how therein, as well as all Intellectual Property or know-how made or developed solely or jointly by Contractor in the course of performing the Services or otherwise under this Agreement (collectively, the "**Project IP**"); provided, however, the Project IP excludes the Contractor Technology. Contractor shall notify PhaseBio in writing of any and all Project IP promptly after its conception, development or reduction to practice. Contractor hereby assigns and transfers to PhaseBio all of its right, title and interest in and to the Project IP and shall take, and to cause its employees, agents, and consultants to take, all further acts reasonably required to evidence such assignment and transfer to PhaseBio, at PhaseBio's reasonable expense. Contractor shall not apply for any patent, copyright, trademark or other statutory or common law protection of any Project IP. PhaseBio may use, assert, and apply for patent, copyright, trademark and other statutory or common law protection for any or all Project IP in any and all countries. Contractor waives and releases, to the extent permitted by law, all rights to the Project IP, and shall assist PhaseBio in every reasonable way, without additional compensation (but at PhaseBio's expense), in PhaseBio's application for, prosecution and obtaining patent, copyright or other protection for Project EP, and in PhaseBio's enforcement, defense and protection from time to time of PhaseBio's rights to Project IP. Contractor shall, whether during or following its engagement hereunder, at PhaseBio's request and expense, but without additional compensation, execute any and all assignments, transfers, applications and other papers covering any and all Project IP which may be considered necessary or helpful by PhaseBio in furtherance of the foregoing and/or to accomplish the assignment, transfer and/or license of any Project IP to PhaseBio or persons or entities designated by PhaseBio. Any assignment of copyright hereunder includes Contractor's rights of attribution, integrity, disclosure and withdrawal and any other rights that may be known as or referred to as "**moral rights**" (collectively, "**Moral Rights**"). To the extent such Moral Rights cannot be assigned under applicable law and to the extent permitted by the laws in the various countries where Moral Rights exist, Contractor hereby waives such Moral Rights. Contractor will confirm any such waivers from time to time as requested by PhaseBio.

7.4 Contractor Technology. Work Product shall not include Contractor Technology, and, as between the parties, all Contractor Technology shall be owned solely by Contractor. In order to provide PhaseBio with freedom to operate with respect to Products, Contractor hereby grants to PhaseBio a limited worldwide, royalty-free, fully-paid, non-exclusive license, including the right to sublicense through multiple tiers of sublicense, under Contractor Technology pertaining to or embodied within the Deliverables or that is actually used by Contractor in the performance of the Services to make, have made, use, sell, have sold, offer for sale and import such Product.

7.5 Technology Transfer. Contractor shall provide reasonable technical assistance and make its technical personnel reasonably available to PhaseBio, as necessary for PhaseBio to implement any processes developed by Contractor during its conduct of the Services or conduct development and commercialization of any Deliverable provided by Contractor. PhaseBio shall compensate Contractor for its reasonable out-of-pocket and personnel costs for providing such technical assistance.

8. CONFIDENTIALITY

8.1 Confidential Information. All information that is disclosed or provided by PhaseBio to Contractor pursuant to this Agreement or pursuant to the Confidentiality Agreement shall be "**Confidential Information**" of PhaseBio. Confidential Information may be disclosed by PhaseBio in oral, written or other tangible form or otherwise learned by Contractor under this Agreement, and may including but not limited to PhaseBio's research, development, preclinical and clinical programs, data and results; pharmaceutical or biologic candidates and products; inventions, works of authorship, trade secrets, processes, conceptions, formulas, patents, patent applications, and licenses; business, product, marketing, sales, scientific and technical strategies, programs and results, including costs and prices; suppliers, manufacturers, customers, market data, personnel, and consultants; and other confidential or proprietary matters related to the Services. Notwithstanding the foregoing, all reports provided under this Agreement, Developments, Deliverables, and Project IP are the Confidential Information of PhaseBio, regardless of which Party disclosed such information. Except to the extent expressly authorized by this Agreement or by PhaseBio in writing, during the Term and for ten (10) years thereafter, Contractor shall maintain in strict trust and confidence and shall not disclose to any third party or use for any purpose other than as provided for in this Agreement any Confidential Information. Contractor may use the Confidential Information only to the extent required to perform the Services and for no other purpose. Contractor shall not use the Confidential Information for any purpose or in any manner that would constitute a violation of Applicable Laws.

8.2 Exceptions. The obligations of confidentiality and nonuse set forth in Section 8.1 shall not apply to any specific portion of information that Contractor can demonstrate by competent evidence: (a) is in the public domain or comes into the public domain through no fault of Contractor; (b) is furnished to Contractor by a third party rightfully in possession of such information not subject to a duty of confidentiality with respect thereto, as shown by Contractor's written records contemporaneous with such third party disclosure; (c) is already known by Contractor at the time of receiving such Confidential Information and as evidenced by Contractor's prior written records, provided further that this exception does not apply to Developments; or (d) is independently developed by Contractor outside of any activities contemplated by this Agreement without use or reference to or reliance upon the Confidential Information, as demonstrated by Contractor's independent written records contemporaneous with such development. Specific aspects or details of Confidential Information shall not be deemed to be within the public domain or in the possession of the receiving Party merely because the Confidential Information is embraced by more general information in the public domain or in the possession of the receiving Party. Further, any combination of Confidential Information shall not be considered in the public domain or in the possession of the receiving Party merely because individual elements of such Confidential Information are in the public domain or in the possession of the receiving Party unless the combination and its principles are in the public domain or in the possession of the receiving Party.

8.3 Authorized Disclosure. Notwithstanding the foregoing in this Section 8, Contractor may disclose certain Confidential Information to the extent such disclosure is required by law or regulation, or pursuant to a valid order of a court or other governmental body having jurisdiction, provided that Contractor provides PhaseBio with reasonable prior written notice of such disclosure and reasonable assistance in obtaining a protective order or confidential treatment preventing or limiting the disclosure or requiring that the Confidential Information so disclosed be used only for the purposes for which the law or regulation required, or for which the order was issued; provided further, that the Confidential Information disclosed pursuant to a requirement of applicable law or an order of a court of competent jurisdiction or a facially valid administrative, Congressional or other subpoena shall be limited to that information which, in the opinion of the receiving Party's legal counsel, is legally required to be disclosed.

8.4 Publication; Use of Names. Under no circumstances may either Party use the name of the other Party or any of its personnel in any publication or any form of advertising without such other Party's prior written consent. For the avoidance of doubt, Contractor may not publish any articles or make any presentations relating to the Services or referring to data, information or materials generated as part of the Services, in whole or in part, without the prior written consent of PhaseBio.

8.5 Third Party Confidential Information. Contractor shall not disclose to PhaseBio any confidential or proprietary information that belongs to any third party unless Contractor first obtains the consent of such third party and enters into a separate confidentiality agreement with PhaseBio covering that disclosure. Contractor shall not represent to PhaseBio as being unrestricted any designs, plans, models, samples, or other writings or products that Contractor knows are covered by valid patent, copyright, or other form of intellectual property protection belonging to a third party.

8.6 Return of Confidential Information. Upon termination or expiration of the Agreement, or upon written request of PhaseBio, Contractor shall promptly return or destroy all documents, notes and other tangible materials representing PhaseBio's Confidential Information and all copies thereof; provided, however, that Contractor may retain a single archival copy of the Confidential Information for the sole purpose of facilitating compliance with the surviving provisions of this Agreement.

8.7 Injunctive Relief. The Parties expressly acknowledge and agree that any breach or threatened breach of this Section 8 by Contractor may cause immediate and irreparable harm to PhaseBio that may not be adequately compensated by damages. Each Party therefore agrees that in the event of such breach or threatened breach by Contractor, and in addition to any remedies available at law, PhaseBio may secure equitable and injunctive relief, without bond, in connection with such a breach or threatened breach.

9. REPRESENTATIONS AND WARRANTIES

9.1 Due Authorization. Each Party represents and warrants that (a) it has the full power and authority to enter into this Agreement, (b) this Agreement has been duly authorized, and (c) this Agreement is binding upon it.

9.2 No Inconsistent Obligations or Constraints upon Contractor. Contractor represents and warrants that (a) it is qualified and permitted to enter into this Agreement; (b) the terms of the Agreement are not inconsistent with its other contractual arrangements; (c) it has the right to grant all licenses granted to PhaseBio in this Agreement; (d) PhaseBio may freely use, practice, reproduce, distribute, make and sell all advice, data, information, inventions, works of authorship or know-how that Contractor conveys or provides to PhaseBio hereunder, in the form of a Deliverable or otherwise, without restriction and without infringing or misappropriating any third party Intellectual Property or other rights; and (e) it shall perform the Services in accordance with the highest standards of care and diligence practiced by recognized firms in providing services of a similar nature.

9.3 No Pending Litigation. Contractor represents and warrants that it is not currently involved in any litigation, and is unaware of any pending litigation proceedings, relating to Contractor's performance of services for any third party.

9.4 No Debarred Person. Contractor represents and warrants that it will not employ, contract with, or retain any person directly or indirectly to perform the Services under this Agreement if such person is under investigation by the FDA for debarment or is presently debarred by the FDA pursuant to the Generic Drug Enforcement Act of 1992, as amended (21 U.S.C. § 301, et seq.). In addition, Contractor represents and warrants that it has not engaged in any conduct or activity that could lead to any such debarment actions. If during the Term, Contractor or any person employed or retained by it to perform the Services (i) comes under investigation by the FDA for a debarment action, (ii) is debarred, or (iii) engages in any conduct or activity that could lead to debarment, Contractor shall immediately notify PhaseBio of same.

9.5 No Infringement. Contractor represents and warrants that it will not, in the course of conducting the Services, infringe or misappropriate, and that neither the Deliverables nor any element thereof will infringe or misappropriate, any intellectual property right of any third party.

9.6 Deliverables. Contractor warrants that the Services performed and the Deliverables will fully conform to the Specifications, requirements, and other terms in the applicable Statement of Work and this Agreement. In the event of a breach of this warranty, Section 4.8 shall control with respect to any Products and the remainder of this Section 9.6 shall apply with respect to all other Services and Deliverables. If such other Service or Deliverable does not conform to the requirements and other terms in the applicable Statement of Work or this Agreement, then without limiting any other rights or remedies, PhaseBio may request that Contractor, and Contractor shall, promptly re-perform the nonconforming Services at no additional charge to PhaseBio; provided, that if Contractor disputes the existence of such breach, then the Parties shall refer such matter to a mutually agreed independent consultant. If the breach has not been cured within [***] after determination of existence of a breach (or such longer period of time as may be reasonably required to allow for cure of such breach), then Contractor shall refund all fees previously paid to Contractor under the applicable Statement of Work, which will automatically terminate upon the expiration of such timeframe.

9.7 Warranty Disclaimer. EXCEPT AS EXPLICITLY SET FORTH IN THIS SECTION 8, EACH PARTY HEREBY DISCLAIMS ALL OTHER WARRANTIES, EXPRESS

OR IMPLIED, INCLUDING, WITHOUT LIMITATION, THE WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE.

10. QUALITY ASSURANCE. Contractor shall perform the Services (a) in a professional manner, consistent with applicable industry standards and practices and in conformance with that level of care and skill ordinarily exercised in similar circumstances by providers of the same or similar services; (b) in compliance with all PhaseBio policies, procedures and instructions provided to Contractor in writing and applicable to the Services which have been provided to and agreed by Contractor in writing, and (c) accordance with the terms of this Agreement, the applicable Statement of Work, and all Applicable Laws. Contractor shall perform services consistent with its Quality Assurance Standard Operating Procedures (SOPs). Contractor agrees that in performing Services hereunder: (i) Contractor shall comply with the U.S. Foreign Corrupt Practices Act, as amended, the UK Bribery Act 2010, as amended, and any other applicable anti-corruption laws and laws for the prevention of fraud, racketeering, money laundering or terrorism (collectively, "**Anti-Corruption Laws**"), and shall not take any action that will, or would reasonably be expected to, cause PhaseBio or its licensors to be in violation of any Anti-Corruption Laws; and (ii) Contractor shall promptly provide PhaseBio with written notice of the following events: (A) upon becoming aware of any breach or violation by Contractor of any representation, warranty or undertaking set forth in clause (i) of this Section 10 or (B) upon receiving a formal notification that it is the target of a formal investigation by a governmental authority for a material violation of any Anti-Corruption Law.

11. INSURANCE. Contractor, at its sole cost and expense, shall secure and maintain in full force and effect throughout the performance of the Services and for [***] thereafter, (i) Workers' Compensation insurance with coverage in accordance with statutory limits, and (ii) Commercial General Liability insurance, including blanket contractual liability with limits of not less than [***]. Certificates evidencing such insurance shall be made available for examination upon request by PhaseBio.

12. INDEMNIFICATION; LIMITATION OF LIABILITY

12.1 By Contractor. Contractor shall indemnify, defend and hold harmless PhaseBio and its affiliates and their respective directors, officers, employees, and agents (the "**PhaseBio Indemnitees**") from and against any and all costs, expenses, liabilities, damages, losses and harm (including reasonable legal expenses and attorneys' fees) arising out of or resulting from any third party suits, claims, actions, or demands (collectively, "**Claims**") to the extent resulting from or caused by: (a) the infringement or misappropriation by any Deliverable of any third party Intellectual Property (except to the extent caused solely by the Materials); (b) the negligence, recklessness or willful misconduct of Contractor or its officers, directors, employees, or agents; or (c) Contractor's breach of its obligations, warranties, or representations under this Agreement, except in each case to the extent that a Claim arises out of or results from the negligence, recklessness or willful misconduct of any PhaseBio Indemnitee or PhaseBio's breach of its obligations, warranties, or representations under this Agreement.

12.2 By PhaseBio. PhaseBio shall indemnify, defend and hold harmless Contractor and its directors, officers, employees, and agents (the "**Contractor Indemnitees**") from and against any and all Claims to the extent resulting from or caused by: (a) the negligence, recklessness or

willful misconduct of any PhaseBio Indemnitee; (b) PhaseBio's breach of its obligations, warranties or representations under this Agreement, or (c) the development, manufacture, use, handling, storage, sale or other disposition of Product by or on behalf of PhaseBio (including any claim by any third party that the development, manufacture, use, handling, storage, sale or other disposition of Product infringes or misappropriates the intellectual property rights of such third party, except to the extent such claim relates solely to Contractor Technology used in connection therewith), except in each case to the extent that a Claim arises out of or results from the negligence, recklessness or willful misconduct of any Contractor Indemnitee or Contractor's breach of its obligations, warranties, or representations under this Agreement.

12.3 Indemnification Conditions and Procedures. Each Party's agreement to indemnify, defend and hold harmless the other Party is conditioned on the indemnified Party: (i) providing written notice to the indemnifying Party of any claim or demand for which it is seeking indemnification hereunder promptly after the indemnified Party has knowledge of such claim; (ii) permitting the indemnifying party to assume full responsibility to investigate, prepare for and defend against any such claim or demand, except that the indemnified Party may cooperate in the defense at its expense using its own counsel; (iii) assisting the indemnifying Party, at the indemnifying Party's reasonable expense, in the investigation of, preparing for and defense of any such claim or demand; and (iv) not compromising or settling such claim or demand without the indemnifying Party's written consent.

12.4 Limitation of Liability. EXCEPT FOR DAMAGES AVAILABLE FOR BREACHES OF CONFIDENTIALITY OBLIGATIONS UNDER SECTION 7 AND THE INDEMNIFICATION RIGHTS AND OBLIGATIONS UNDER SECTION 10, NEITHER PARTY SHALL BE LIABLE TO THE OTHER PARTY FOR ANY SPECIAL, CONSEQUENTIAL, INCIDENTAL, PUNITIVE OR INDIRECT DAMAGES ARISING FROM OR RELATING TO ANY BREACH OF THIS AGREEMENT, REGARDLESS OF ANY NOTICE OF THE POSSIBILITY OF SUCH DAMAGES.

13. TERM AND TERMINATION

13.1 Term. The term of this Agreement (the "**Term**") shall commence on the Effective Date and continue thereafter until terminated in accordance with this Section 13.

13.2 Termination by PhaseBio. PhaseBio may terminate this Agreement or any Statement of Work at any time with or without cause for its convenience, effective upon [***] notice to Contractor.

13.3 Termination by Contractor. Contractor may terminate this Agreement at any time with or without cause for its convenience, effective upon [***] notice to PhaseBio, provided that termination will not be effective until the last remaining Statement of Work is complete.

13.4 Termination for Cause. A Party may terminate this Agreement or any Statement of Work for material breach of this Agreement by the other Party upon [***] written notice specifying the nature of the breach, if such breach has not been cured within such [***] period. If such notice of breach is for breach of a Statement of Work, such notice shall note the specific Statement of Work under which such breach is claimed.

13.5 Effects of Termination

13.5.1 Survival. Sections 1, 2.11, 3, 5.1, 6, 7, 8, 10, 11 (solely to the extent the Claims can be attributed to action or omission during the Term), 13.3 and 14 shall survive any termination or expiration of this Agreement. Termination or expiration of this Agreement shall not affect either Party's liability for any breach of this Agreement it may have committed before such expiration or termination.

13.5.2 Return of PhaseBio Property. Upon termination of this Agreement, Contractor shall return or destroy the Materials, and return to PhaseBio the Confidential Information, as set forth in Sections 2.11 and 8.6. In addition, Contractor shall deliver to PhaseBio, or destroy at PhaseBio's request, the Deliverables (in whatever stage of development or completion).

13.6 **Payment.** Upon termination or expiration of this Agreement or termination of any Statement of Work, neither Contractor nor PhaseBio shall have any further obligations under this Agreement or such Statements of Work, except as set forth in Section 13.5 and except that, with respect to each terminated Statement of Work:

13.6.1 Contractor shall terminate all Services in progress, including subcontracted Services, in an orderly manner as soon as practical and in accordance with a schedule agreed to by PhaseBio, unless PhaseBio specifies in the notice of termination that Services in progress should be completed;

13.6.2 Contractor shall deliver to PhaseBio all Materials, Deliverables and Work Product not previously delivered to PhaseBio, Product, retained samples (except for samples Contractor is required to retain pursuant to applicable law), records, data, reports and other property, information, and know-how in recorded form that was provided by PhaseBio, or developed in the performance of the Services;

13.6.3 Contractor shall use commercially reasonable efforts to return to the vendor for a refund all unused, returnable materials in Contractor's possession that are related to any such Statements of Work;

13.6.4 within [***] after the termination of any Statements of Work, Contractor shall provide to PhaseBio a written itemized cost statement of all Services performed in connection with the terminated Statements of Work and a final invoice for such Statements of Work, pursuant to the terms and conditions set forth in such Statement of Work. If PhaseBio has paid to Contractor in advance more than the amount in a final invoice, then Contractor shall refund the excess payment to PhaseBio, or to credit the excess payment toward any other existing or future Statements of Work, at the election of PhaseBio.

14. GENERAL PROVISIONS

14.1 **Governing Law; Venue.** This Agreement is governed by the laws of the State of Delaware without reference to any conflict of laws principles that would require the application of the laws of any other jurisdiction. The United Nations Convention on Contracts for the International Sale of Goods does not apply to this Agreement. Contractor irrevocably consents to

the personal jurisdiction of the state and federal courts located in Philadelphia, Pennsylvania for any suit or action arising from or related to this Agreement, and waives any right Contractor may have to object to the venue of such courts. Contractor further agrees that these courts will have exclusive jurisdiction over any such suit or action initiated by Contractor against PhaseBio.

14.2 Severability. If any provision of this Agreement is, for any reason, held to be invalid or unenforceable, the other provisions of this Agreement will be unimpaired and the invalid or unenforceable provision will be deemed modified so that it is valid and enforceable to the maximum extent permitted by law.

14.3 Limitation of Liability. EXCEPT FOR DAMAGES AVAILABLE FOR BREACHES OF CONFIDENTIALITY OBLIGATIONS UNDER SECTION 7 AND THE INDEMNIFICATION RIGHTS AND OBLIGATIONS UNDER SECTION 11, IN NO EVENT SHALL EITHER PARTY BE LIABLE FOR INDIRECT, SPECIAL, CONSEQUENTIAL, OR INCIDENTAL DAMAGES INCLUDING, BUT NOT LIMITED TO DAMAGES FOR LOSS OF PROFIT OR GOODWILL REGARDLESS OF WHETHER SUCH PARTY HAS BEEN INFORMED OF THE POSSIBILITY OF SUCH DAMAGES. Notwithstanding anything to the contrary stated in this Agreement or any attachments thereto, in no event shall Contractor be liable to PhaseBio for any and all causes, whether based in contract or in tort, including negligence, strict liability, or any other cause, that in the aggregate exceeds twice the amount of the total fees paid to Contractor by PhaseBio under the applicable work order giving rise to such liability.

14.4 No Assignment. Neither Party shall assign this Agreement to any other person or entity without the prior written consent of the other, and any purported assignment without such consent shall be void, provided however, that PhaseBio may assign this Agreement without such consent (a) to an Affiliate, (b) in connection with the transfer or sale of all or substantially all of PhaseBio's business to which this Agreement relates to a third party, whether by merger, sale of stock, sale of assets or otherwise, or (c) to PhaseBio's licensor of PB2452 and such licensor's affiliated entities (collectively, "**Licensor**") in the event of termination of the license granted by Licensor to PhaseBio. This Agreement shall be binding upon and shall inure to the benefit of the Parties hereto and their respective successors and permitted assigns.

14.5 Notices. Each Party must deliver all notices, consents, and approvals required or permitted under this Agreement in writing to the other Party at the address specified below, by personal delivery, by certified or registered mail (postage prepaid and return receipt requested), by a nationally-recognized overnight carrier, or by electronic mail with confirmation of transmission. Notice will be effective upon receipt or refusal of delivery. Each Party may change its address for receipt of notice by giving notice of such change to the other Party.

If to PhaseBio:

PhaseBio Pharmaceuticals, Inc.
1 Great Valley Parkway
Suite 30
Malvern, Pennsylvania 19355 United States
Attention: CFO/Legal
E-mail: john.sharp@phasebio.com

If to Contractor:

BioVectra Inc.
11 Aviation Avenue
Charlottetown, PE, C1E 0A1, Canada
Attention: Legal Department
E-mail: vdeighan@biovectra.com

14.6 Remedies. The rights and remedies provided to each Party in this Agreement are cumulative and in addition to any other rights and remedies available to such Party at law or in equity.

14.7 Construction. Section headings are included in this Agreement merely for convenience of reference; they are not to be considered part of this Agreement or used in the interpretation of this Agreement. No rule of strict construction will be applied in the interpretation or construction of this Agreement.

14.8 Waiver. All waivers must be in writing and signed by the Party to be charged. Any waiver or failure to enforce any provision of this Agreement on one occasion will not be deemed a waiver of any other provision or of such provision on any other occasion.

14.9 Time Is of the Essence. Time is of the essence in the performance of the Services and Contractor's other obligations under this Agreement.

14.10 Entire Agreement; Amendments. This Agreement, including the Statements of Work hereunder, is the final, complete, and exclusive agreement of the Parties with respect to the subject matter hereof and supersedes and merges all prior or contemporaneous communications and understandings between the Parties. No modification of or amendment to this Agreement will be effective unless in writing and signed by the Party to be charged.

14.11 Counterparts. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original and all of which shall constitute together the same instrument.

Signature Page to Follow

IN WITNESS WHEREOF, the Parties have executed this Master Services Agreement as of the Effective Date.

PHASEBIO PHARMACEUTICALS, INC.

Signed: /s/Susan Arnold
Name: Susan Arnold
Title: VP, Preclinical & CMC

BIOVECTRA INC.

Signed: /s/Heather Delage
Name: Heather Delage
Title: VP Business Development

Signature Page to Master Services Agreement

Consent of Independent Registered Public Accounting Firm

The Board of Directors
PhaseBio Pharmaceuticals, Inc.:

We consent to the incorporation by reference in the registration statement (No. 333-227935) on Form S-8 of PhaseBio Pharmaceuticals, Inc. of our report dated March 26, 2019, with respect to the balance sheets of PhaseBio Pharmaceuticals, Inc. as of December 31, 2018 and 2017, the related statements of operations, redeemable convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the years then ended, and the related notes (collectively, the financial statements), which report appears in the December 31, 2018 annual report on Form 10-K of PhaseBio Pharmaceuticals, Inc.

/s/ KPMG

Philadelphia, Pennsylvania
March 26, 2019

**CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, Jonathan P. Mow, certify that:

1. I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2018 of PhaseBio Pharmaceuticals, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 26, 2019

By: /s/ Jonathan P. Mow
Jonathan P. Mow
Chief Executive Officer

**CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002**

I, John Sharp, certify that:

1. I have reviewed this Annual Report on Form 10-K for the year ended December 31, 2018 of PhaseBio Pharmaceuticals, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 26, 2019

By: /s/ John Sharp
John Sharp
Chief Financial Officer

**CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report on Form 10-K of PhaseBio Pharmaceuticals, Inc. (“the Company”) for the period ended December 31, 2018, as filed with the Securities and Exchange Commission on the date hereof (the “Report”), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that, to the best of his knowledge:

- (1) The Report fully complies with the requirements of Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934, as amended; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 26, 2019

By: /s/ Jonathan P. Mow

Jonathan P. Mow
Chief Executive Officer

The foregoing certification is being furnished solely to accompany the Report pursuant to 18 U.S.C. § 1350, and is not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and is not to be incorporated by reference into any filing of the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing. A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

**CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report on Form 10-K of PhaseBio Pharmaceuticals, Inc. (the "Company") for the period ending December 31, 2018 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that, to the best of her knowledge:

- (1) The Report fully complies with the requirements of Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934; as amended; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 26, 2019

By: /s/ John Sharp

John Sharp
Chief Financial Officer

The foregoing certification is being furnished solely to accompany the Report pursuant to 18 U.S.C. § 1350, and is not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and is not to be incorporated by reference into any filing of the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing. A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.