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

FORM 10-Q

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

For the quarterly period ended March 31, 2019

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	**03-0375697**
(State or other jurisdiction of incorporation or organization)	**(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)

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

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

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

Securities registered or to be registered pursuant to Section 12(b) of the Act.

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock	PHAS	The Nasdaq Stock Market LLC

Class of Common Stock	**Outstanding Shares as of May 3, 2019**
Common Stock, $0.001 par value	28,626,950

Table of Contents

PART 1. FINANCIAL INFORMATION

Item 1. Financial Statements

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

	March 31, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 51,894	$ 61,031
Restricted cash	20	20
Other receivable	670	233
Prepaid expenses and other assets	1,491	1,344
Total current assets	54,075	62,628
Property and equipment, net	380	355
Operating lease right-of-use assets	1,899	—
Other assets	32	43
Total assets	$ 56,386	$ 63,026
Liabilities and stockholders' equity		
Current liabilities:		
Current portion of long-term debt	$ 423	$ -
Accounts payable	2,058	1,806
Accrued expenses and other current liabilities	1,316	2,771
Total current liabilities	3,797	4,577
Long-term debt	6,841	7,500
Operating lease liabilities	1,666	—
Deferred rent	—	22
Total liabilities	12,304	12,099
Commitments and contingencies (*Note 7*)		
Stockholders’ equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized at March 31, 2019 and December 31, 2018; zero shares issued and outstanding at March 31, 2019 and December 31, 2018	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized; 24,528,392 shares issued and 24,498,425 shares outstanding at March 31, 2019; 24,528,242 shares issued and 24,498,275 shares outstanding at December 31, 2018	25	25
Treasury stock, at cost, 29,967 shares as of March 31, 2019 and December 31, 2018	(24)	(24)
Additional paid-in capital	174,285	173,837
Accumulated deficit	(130,204)	(122,911)
Total stockholders’ equity	44,082	50,927
Total liabilities and stockholders' equity	$ 56,386	$ 63,026

See accompanying notes to unaudited condensed financial statements.

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

	Three Months Ended March 31,	
	2019	2018
Grant revenue	$ 653	$ —
Operating expenses:		
Research and development	5,721	2,235
General and administrative	2,316	643
Total operating expenses	8,037	2,878
Loss from operations	(7,384)	(2,878)
Other income (expense):		
Interest income	317	36
Interest expense	(226)	(1,404)
Change in fair value of warrant liability	—	5
Change in fair value of derivative liability	—	(162)
Total other income (expense)	91	(1,525)
Net loss	$ (7,293)	$ (4,403)
Net loss per common share, basic and diluted	$ (0.30)	$ (5.90)
Weighted average common shares outstanding, basic and diluted	24,498,388	745,812

See accompanying notes to unaudited condensed financial statements.

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

	Redeemable Convertible Preferred Stock		Stockholders' Equity (Deficit)						
			Common Stock		Treasury Stock		Additional Paid-in	Accumulated	Total Stockholders'
	Shares	Amount	Shares	Amount	Shares	Amount	Capital	Deficit	Equity (Deficit)
Balance at December 31, 2018	—	$ —	24,528,242	$ 25	(29,967)	$ (24)	$ 173,837	$ (122,911)	$ 50,927
Issuance of common stock warrants	—	—	—	—	—	—	210	—	210
Exercises of stock options	—	—	150	—	—	—	—	—	—
Stock-based compensation	—	—	—	—	—	—	238	—	238
Net loss	—	—	—	—	—	—	—	(7,293)	(7,293)
Balance at March 31, 2019	—	$ —	24,528,392	$ 25	(29,967)	$ (24)	$ 174,285	$ (130,204)	$ 44,082
Balance at December 31, 2017	9,132,024	$ 89,634	775,780	$ 9	(29,967)	$ (24)	$ 1,664	$ (99,065)	$ (97,416)
Stock-based compensation	—	—	—	—	—	—	104	—	104
Accretion of redeemable preferred stock to redemption value	—	16	—	—	—	—	(16)	—	(16)
Net loss	—	—	—	—	—	—	—	(4,403)	(4,403)
Balance at March 31, 2018	9,132,024	$ 89,650	775,780	$ 9	(29,967)	$ (24)	$ 1,752	$ (103,468)	$ (101,731)

See accompanying notes to unaudited condensed financial statements.

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

	Three Months Ended March 31,	
	2019	2018
Operating activities		
Net loss	$ (7,293)	$ (4,403)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	31	27
Stock-based compensation	238	104
Non-cash interest expense	129	1,365
Change in fair value warrant liability	—	(5)
Change in fair value derivative liability	—	162
Changes in operating assets and liabilities:		
Other receivable	(437)	—
Prepaid expenses and other assets	(99)	246
Accounts payable	225	129
Accrued expenses	(1,533)	(257)
Deferred rent	8	(2)
Net cash used in operating activities	(8,731)	(2,634)
Investing activities		
Purchases of property and equipment	(84)	(6)
Net cash used in investing activities	(84)	(6)
Financing activities		
Long-term borrowings, net	616	—
Repayments of long-term debt	(938)	—
Net cash used in financing activities	(322)	—
Net decrease in cash and cash equivalents	(9,137)	(2,640)
Cash, cash equivalents and restricted cash at the beginning of the period	61,051	13,406
Cash, cash equivalents and restricted cash at the end of the period	$ 51,914	$ 10,766
Supplemental disclosure for cash flow		
Cash paid for interest	$ 98	$ 39
Supplemental disclosure of non-cash investing and financing activities		
Accrued interest on term loan refinanced to principal	$ 308	$ —
Issuance of warrants in conjunction with debt	$ 209	$ —
Debt refinanced with new term loan	$ 6,563	$ —
Initial recognition of operating lease right-of-use assets and operating lease liabilities	$ 1,991	$ —
Accretion of redeemable convertible preferred stock	$ —	$ 16
Purchases of property and equipment included in accounts payable	$ 11	$ 10

See accompanying notes to unaudited condensed 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'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 technology, which also serves as the engine for our preclinical pipeline.

Initial Public Offering

In October 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 $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 condensed financial statements for all periods presented to reflect the reverse stock split. Further, exercise prices of stock options have been retroactively adjusted in these condensed 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 March 31, 2019, had an accumulated deficit of $130.2 million. The Company expects to continue to incur net losses for at least the next several years. As of March 31, 2019, the Company had cash and cash equivalents of $51.9 million and working capital of $50.3 million. In April 2019, the Company completed an underwritten public offering of its common stock, which resulted in the issuance and sale of an aggregate of 4,124,475 shares of common stock at a public offering price of $12.00 per share, generating net proceeds of $46.2 million after deducting underwriting discounts and commissions and other offering costs (see Note 14). Management believes that its cash and cash equivalents as of March 31, 2019, together with the net proceeds from the April 2019 offering, are sufficient to fund the Company's operating expenses and capital requirements into the second half of 2020.

Basis of Presentation

The accompanying condensed financial statements have been prepared in accordance with U.S. generally accepted accounting principles ("GAAP") for interim financial reporting and the rules and regulations of the Securities and Exchange Commission ("SEC"). Certain information and note disclosures normally included in annual financial statements prepared in accordance with GAAP have been condensed or omitted pursuant to those rules and regulations. All adjustments, consisting only of normal recurring adjustments, necessary for a fair presentation of the accompanying condensed financial statements have been made. Although these interim financial statements do not include all of the information and footnotes required for complete annual financial statements, management believes the disclosures are adequate to make the information presented not misleading. The unaudited interim results of operations and cash flows for the three months ended March 31, 2019 are not necessarily indicative of the results that may be expected for the full year. The unaudited interim condensed financial statements and footnotes should be read in conjunction with the audited

financial statements and footnotes for the year ended December 31, 2018, included in the Company's Annual Report on Form 10-K for the year ended December 31, 2018, filed with the SEC on March 26, 2019, wherein a more complete discussion of significant accounting policies and certain other information can be found.

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 condensed 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 condensed financial statements and accompanying notes. The most significant estimates in the Company's condensed financial statements relate to the valuation of redeemable convertible preferred stock warrants prior to the IPO, the conversion option on the convertible notes prior to conversion 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 deposit accounts and money market funds 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 March 31, 2019 and December 31, 2018, 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 other receivable, prepaid expenses and other assets, accounts payable and accrued expenses and other current liabilities 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 values of the term loan and operating lease liabilities and corresponding right-of-use assets approximate their respective carrying values.

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.

Leases

At lease commencement, the Company records a lease liability based on the present value of lease payments over the expected

lease term including any options to extend the lease that the Company is reasonably certain to exercise. The Company calculates the present value of lease payments using an incremental borrowing rate as the Company's leases do not provide an implicit interest rate. The Company's incremental borrowing rate for a lease is the rate of interest it would have to pay on a collateralized basis to borrow an amount equal to the lease payments under similar terms. At the lease commencement date, the Company records a corresponding right-of-use lease asset based on the lease liability, adjusted for any lease incentives received and any initial direct costs paid to the lessor prior to the lease commencement date. The Company may enter into leases with an initial term of 12 months or less ("Short-Term Leases"). For Short-Term Leases, the Company records the rent expense on a straight-line basis and does not record the leases on the condensed balance sheet. The Company had no Short-Term Leases as of March 31, 2019 or December 31, 2018.

After lease commencement, the Company measures its leases as follows: (i) the lease liability based on the present value of the remaining lease payments using the discount rate determined at lease commencement and (ii) the right-of-use lease asset based on the remeasured lease liability, adjusted for any unamortized lease incentives received, any unamortized initial direct costs and the cumulative difference between rent expense and amounts paid under the lease agreement. Any lease incentives received and any initial direct costs are amortized on a straight-line basis over the expected lease term. Rent expense is recorded on a straight-line basis over the expected 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 and right-of-use assets 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 did not recognize any impairment losses in either the three months ended March 31, 2019 or the year ended December 31, 2018.

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 condensed 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 condensed 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, contract manufacturing 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 condensed 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 also maintains an employee stock purchase program under which it may issue shares. 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 and records forfeitures in the period in which they occur.

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 (for option grants 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 condensed financial statements. Under this method, deferred tax assets and liabilities are determined on the basis of the differences between the condensed 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 Revenue

Grant revenue is 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.

	As of March 31,	
	2019	2018
Redeemable convertible preferred stock	—	9,132,024
Common stock options	2,525,055	1,075,284
Warrants to purchase common stock	113,203	—
Warrants to purchase redeemable convertible preferred stock	—	484,860
Total	2,638,258	10,692,168

Recent Accounting Pronouncements

In February 2016, the FASB issued ASU 2016-02, *Leases*. This update amended the current accounting guidance for lease transactions. Under the new guidance, a lessee is required to recognize both assets and liabilities for any leases in excess of twelve months. Additionally, certain qualitative and quantitative disclosures are required in the financial statements. The Company adopted ASU 2016-02 in the first quarter of 2019 using a modified retrospective transition method as of the effective date as permitted by the amendments in ASU 2018-11. As a result, the Company was not required to adjust comparative period financial information for effects of the standard or make the new required lease disclosures for periods before the date of adoption. The Company has elected to adopt the package of transition practical expedients and, therefore, has not reassessed (1) whether existing or expired contracts contain a lease, (2) lease classification for existing or expired leases or (3) the accounting for initial direct costs that were previously capitalized. The Company did not elect the practical expedient to use hindsight for leases existing at the adoption date. Further, the Company does not expect the amendments in ASU 2018-01: Land Easement Practical Expedient to have an effect on us because the Company does not enter into land easement arrangements. There was no effect of the adoption of Topic 842 on retained earnings and other components of equity as of December 31, 2018. Upon adoption, the Company recorded right-of-use assets and corresponding lease liabilities of $2.0 million.

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 March 31, 2019:				
Assets				
Cash equivalents	$ 49,673	$ 49,673	$ —	$ —
As of December 31, 2018:				
Assets				
Cash equivalents	$ 59,357	$ 59,357	$ —	$ —

4. Property and Equipment

The following table presents the composition of property and equipment, net as of March 31, 2019 and December 31, 2018 (in thousands):

	As of March 31, 2019	As of December 31, 2018
Lab equipment	$ 1,781	$ 1,764
Computer hardware, software and telephone	253	228
Furniture and fixtures	98	98
Leasehold improvements	64	50
	2,196	2,140
Less accumulated depreciation	(1,816)	(1,785)
Property and equipment, net	$ 380	$ 355

5. Accrued Expenses

The following table presents the composition of accrued expenses as of March 31, 2019 and December 31, 2018 (in thousands):

	As of March 31, 2019	As of December 31, 2018
Accrued clinical and related costs	$ 447	$ 1,358
Accrued compensation and related costs	401	914
Accrued interest	10	194
Operating lease liability, short-term	262	—
Accrued other	196	305
Accrued expenses and other current liabilities	$ 1,316	$ 2,771

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 (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 zero and $1.3 million for the three months ended March 31, 2019 and 2018, respectively.

Term Loans

October 2017 Loan Agreement with Silicon Valley Bank

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.

March 2019 Loan Agreement with Silicon Valley Bank and WestRiver Innovation Lending Fund VIII, L.P.

In March 2019, the Company entered into a new 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 (“Tranche 1”), which was issued upon execution of the 2019 Loan, $2.5 million available to be issued until May 31, 2019 (“Tranche 2”) and $5.0 million (“Tranche 3”), which the Company will draw upon the achievement of certain regulatory milestones (the “Tranche 3 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 1 and Tranche 2 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 until paid in full. The interest-only period will automatically be extended to June 30, 2020 if the Company achieves the Tranche 3 milestones, followed by an amortization period of 33 months of equal monthly payments of principal plus interest 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 (“Final Payment”) on the maturity date.

Upon execution of the 2019 Loan and the draw of Tranche 1, the Company issued to SVB and WestRiver warrants to purchase an aggregate of 37,606 shares of common stock with an exercise price of $4.73 per share. The Company has agreed to issue additional warrants to SVB and WestRiver to purchase an aggregate of 12,131 and 24,262 shares of common stock upon the draw of Tranche 2 and Tranche 3, respectively, 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.

Upon execution of the 2019 Loan, the Company drew $7.5 million from Tranche 1 and repaid the outstanding principal balance and the accrued portion of the Final Payment of the SVB Loan.

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.

The Company recorded a debt discount of $0.2 million for the estimated fair value of warrants and debt issuance costs upon the borrowing of Tranche 1, which is being amortized to interest expense over the term of the 2019 Loan using the effective-interest method. Interest expense, including amortization of the debt discount related to the term debt, totaled $0.2 million and $0.1 million for the three months ended March 31, 2019 and 2018, respectively. The balance of the Final Payment liability was $4,000 as of March 31, 2019 and is included in long-term debt on the condensed balance sheet. The Company is in compliance with all covenants under the 2019 Loan as of March 31, 2019.

Based on a 39-month amortization of the outstanding principal amounts for the 2019 Loan as discussed above, the following table sets forth by year the Company's required future principal payments (in thousands):

Years Ending December 31,	
2019 (remaining nine months)	$ —
2020	2,139
2021	2,285
2022	2,441
2023	635
Thereafter	—
	$ 7,500

7. Commitments and Contingencies

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 entered into a master services agreement ("Supply Agreement") with BioVectra Inc., ("BioVectra"). BioVectra will manufacture and supply cGMP-grade quantities of PB2452 for the Company's potential Phase 3 clinical trial as well as any work required to support the marketing authorization filing of PB2452. The Company plans to put a commercial supply agreement in place for PB2452 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 a majority of the 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. Leases

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 July 31, 2018 and again to September 30, 2023, with an option to extend the lease for an additional three years. 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. As of March 31, 2019, the weighted average remaining lease term for the Company's leases was 6.7 years, and the weighted average discount rate used to determine the right-of-use assets and corresponding operating lease liabilities was 6.4%.

Maturities of operating lease liabilities as of March 31, 2019 are as follows (in thousands):

Year Ending December 31,	
2019 (remaining nine months)	$ 254
2020	372
2021	377
2022	363
2023	272
Thereafter	776
Total future lease payments	2,414
Less: Present value adjustment	(486)
Operating lease liabilities	$ 1,928

The Company recognizes rent expense for the operating leases on a straight-line basis. The Company accounts for the cumulative difference between the minimum lease payments and the straight-line amount as deferred rent and records it as an offset to operating lease right-of-use assets. Rent expense was $0.1 million for each of the three months ended March 31, 2019 and 2018.

9. Stockholders' Equity

Preferred Stock

The Company issued Series 1 redeemable convertible preferred stock, Series 2 redeemable preferred stock, Series AA redeemable convertible preferred stock, Series B redeemable convertible preferred stock, Series C-1 redeemable convertible preferred stock, Series C-2 redeemable convertible preferred stock, Series C-3 redeemable convertible preferred stock, and Series D convertible preferred stock (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.

10. Stock-Based Compensation

Stock-based compensation expense has been reported in the Company's condensed statements of operations for the three months ended March 31, 2019 and 2018 as follows (in thousands):

	Three Months Ended March 31,	
	2019	**2018**
General and administrative	$ 192	$ 28
Research and development	46	76
Total stock-based compensation	$ 238	$ 104

As of March 31, 2019, the total unrecognized compensation expense related to unvested employee and non-employee stock option awards was $3.4 million, which was expected to be recognized in expense over a weighted-average period of approximately 3.2 years.

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 upon the achievement of clinical development and regulatory milestones. As of March 31, 2019, 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, 2018, 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 three months ended March 31, 2019 and 2018. AstraZeneca plc ("AstraZeneca") 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 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 March 31, 2019, 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 March 31, 2019.

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 must pay Duke the first $1.0 million of non-royalty 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 $0.1 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 and zero under the SBIR grants in the three months ended March 31, 2019 and 2018, respectively.

13. Related Party Transactions

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

14. Subsequent Events

April 2019 Offering

In April 2019, the Company completed an underwritten public offering of its common stock, which resulted in the issuance and sale of an aggregate of 4,124,475 shares of common stock at a public offering price of $12.00 per share, generating net proceeds of $46.2 million after deducting underwriting discounts and commissions and other offering costs.

Wacker License Agreement

In April 2019, the Company entered into a license agreement (the "Wacker License Agreement") with Wacker Biotech gmbH ("Wacker"), pursuant to which Wacker granted the Company an exclusive license under certain of Wacker's intellectual property rights to use Wacker's proprietary *E. coli* strain for the manufacture of PB2452 worldwide outside of specified Asian countries, and to commercialize PB2452, if approved, manufactured by or on behalf of the Company using Wacker's proprietary *E. coli* strain throughout the world. The Company has the right to grant sublicenses under the license, subject to certain conditions as specified in the Wacker License Agreement. Under the terms of the agreement, the Company is required to pay a fixed nominal per-unit royalty, which is subject to adjustment, and an annual license fee in a fixed Euro amount in the low to mid six digits. The agreement will be in force for an indefinite period of time, and upon the expiration of the Company's royalty obligations, the license will be considered fully paid and will convert to a non-exclusive license. Either party may terminate the Wacker License Agreement for breach if such breach is not cured within a specified number of days.

Item 2. 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 unaudited condensed financial statements and related notes included in this Quarterly Report on Form 10-Q and the audited financial statements and notes thereto as of and for the periods ended December 31, 2018 and 2017 and the related Management's Discussion and Analysis of Financial Condition and Results of Operations, included in our Annual Report on Form 10-K filed with the SEC on March 26, 2019. Unless the context requires otherwise, references in this Quarterly Report on Form 10-Q to "we," "us," and "our" refer to PhaseBio Pharmaceuticals, Inc.

Forward-Looking Statements

The information in this discussion contains forward-looking statements and information within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, which are subject to the "safe harbor" created by those sections. These forward-looking statements include, but are not limited to, statements concerning our strategy, future operations, future financial position, future revenues, projected costs, prospects and plans and objectives of management. The words "anticipates," "believes," "estimates," "expects," "intends," "may," "plans," "projects," "will," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions, or expectations disclosed in our forward-looking statements and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements that we make. These forward-looking statements involve risks and uncertainties that could cause our actual results to differ materially from those in the forward-looking statements, including, without limitation, the risks set forth in Part II, Item 1A, "Risk Factors" in this Quarterly Report on Form 10-Q and in our other filings with the SEC. The forward-looking statements are applicable only as of the date on which they are made, and we do not assume any obligation to update any forward-looking statements.

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. In our recently completed Phase 1 clinical trial of PB2452, 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 dosing cohorts in which we administered PB2452 over an extended infusion period. We began enrollment in our Phase 2a clinical trial of PB2452 in healthy older subjects in April 2019. The United States Food and Drug Administration, or FDA, granted Breakthrough Therapy designation for PB2452 in April 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.

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 financed 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, or our IPO, and the sale of Series D convertible preferred stock and $4.0 million under our term loan with SVB. In April 2019, we received $46.2 million in aggregate net proceeds from an underwritten public offering of our common stock.

Since our inception, we have incurred significant operating losses. Our net loss was $7.3 million for the three months ended March 31, 2019. As of March 31, 2019, we had an accumulated deficit of $130.2 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 any potentially 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 possible future commercialization efforts; and
- incur additional legal, accounting and other expenses in operating as a public company.

Recent Developments

Breakthrough Therapy Designation

In April 2019, the FDA granted Breakthrough Therapy designation for PB2452 for the reversal of ticagrelor's antiplatelet activity. The Breakthrough Therapy designation was supported by our Phase 1 clinical trial results, in which we observed immediate and sustained reversal of ticagrelor's antiplatelet activity.

April 2019 Offering

In April 2019, we completed an underwritten public offering of our common stock, which resulted in the issuance and sale of an aggregate of 4,124,475 shares of common stock at a public offering price of $12.00 per share, generating net proceeds of $46.2 million after deducting underwriting discounts and commissions and other offering costs.

FINANCIAL OVERVIEW

Components of Operating Results

Grant Revenue

Grant revenue is 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
- facilities, 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 potentially 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 our 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 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 by between $1.0 million and $2.0 million on an annual basis.

Interest Expense

Interest expense consists of interest expense on our convertible promissory notes and term loan. Following the conversion of the convertible promissory notes into shares of redeemable convertible Series D preferred stock in August 2018, we no longer recognize interest on the convertible promissory notes. We recognize interest on our term loan with SVB and WestRiver.

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. Following the conversion of our convertible promissory notes to preferred stock in August 2018, the conversion of all outstanding shares of our preferred stock into common stock, and the corresponding conversion of all outstanding preferred stock warrants into common stock warrants, in connection with the closing of our IPO in October 2018, we no longer remeasure the warrant liability or derivative liability for periods following the closing of the IPO.

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 March 31, 2019, 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 April 2019. 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 March 31, 2019, 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.

Wacker License Agreement

In April 2019, we entered into a license agreement, or the Wacker License Agreement, with Wacker Biotech gmbH, or Wacker, pursuant to which Wacker granted us an exclusive license under certain of Wacker's intellectual property rights to use Wacker's proprietary *E. coli* strain for the manufacture of PB2452 worldwide outside of specified Asian countries, and to commercialize PB2452, if approved, manufactured by us or on our behalf using Wacker's proprietary *E. coli* strain throughout the world. We have the right to grant sublicenses under the license, subject to certain conditions as specified in the Wacker License Agreement. Under the terms of the agreement, we are required to pay a fixed nominal per-unit royalty, which is subject to adjustment, and an annual license fee in a fixed Euro amount in the low to mid six digits. The agreement will be in force for an indefinite period of time, and upon the expiration of our royalty obligations, the license will be considered fully paid and will convert to a non-exclusive license. Either party may terminate the Wacker License Agreement for breach if such breach is not cured within a specified number of days

Results of Operations

Comparison of the Three Months Ended March 31, 2019 and 2018

The following table summarizes our results of operations for the three months ended March 31, 2019 and 2018 (in thousands):

	Three Months Ended March 31,		
	2019	2018	Change
Grant revenue	$ 653	$ —	$ 653
Operating expenses:			
Research and development	5,721	2,235	3,486
General and administrative	2,316	643	1,673
Total operating expenses	8,037	2,878	5,159
Loss from operations	(7,384)	(2,878)	(4,506)
Other income (expense):			
Interest income	317	36	281
Interest expense	(226)	(1,404)	1,178
Change in fair value of warrant liability	—	5	(5)
Change in fair value of derivative liability	—	(162)	162
Total other income (expense)	91	(1,525)	1,616
Net loss	$ (7,293)	$ (4,403)	$ (2,890)

Grant Revenue

Grant revenue was $0.7 million for the three months ended March 31, 2019 as we incurred allowable costs qualifying for reimbursement under our government grants. We did not receive any grant revenue for the three months ended March 31, 2018 as we did not receive any grants until the third quarter of 2018.

Research and Development Expense

Research and development expense was $5.7 million for the three months ended March 31, 2019, compared to $2.2 million for the three months ended March 31, 2018. The increase of $3.5 million was primarily attributable to increased costs associated with preclinical and clinical development activities largely related to PB2452.

The following table summarizes our research and development expenses by functional area for the three months ended March 31, 2019 and 2018 (in thousands):

	Three Months Ended March 31,		
	2019	2018	Change
Preclinical and clinical development	$ 4,314	$ 1,367	$ 2,947
Compensation and related benefits	1,085	632	453
Stock-based compensation	46	76	(30)
Facilities expense	158	99	59
Other	118	61	57
Total research and development expenses	$ 5,721	$ 2,235	$ 3,486

We track our external research and development expenses on a program-by-program basis. However, we do not track our internal research and development expenses on a program-by-program basis as they primarily relate to compensation, early research and consumable costs, which are deployed across multiple projects under development. The following table summarizes our research and development expenses by product candidate for the three months ended March 31, 2019 and 2018 (in thousands):

	Three Months Ended March 31,		
	2019	2018	Change
External research and development expense by program:			
PB2452	$ 3,317	$ 307	$ 3,010
PB1046	901	918	(17)
Unallocated research and development expense:			
Compensation and stock-based compensation	1,131	708	423
Other research and development	372	302	70
Total research and development expenses	$ 5,721	$ 2,235	$ 3,486

General and Administrative Expense

General and administrative expense was $2.3 million for three months ended March 31, 2019, compared to $0.6 million for the three months ended March 31, 2018. The increase of $1.7 million was primarily attributable to increases in professional services including legal, marketing and other consulting services, personnel expense due to additional headcount and expenses associated with being a public company.

Interest Expense

Interest expense was $0.2 million for the three months ended March 31, 2019, compared to $1.4 million for the three months ended March 31, 2018. The decrease of $1.2 million was attributable to interest from $13.1 million in borrowings pursuant to our convertible promissory notes, which were outstanding as of March 31, 2018. These notes were converted into shares of redeemable convertible Series D stock in August 2018 and therefore were not outstanding during the three months ended March 31, 2019.

Change in Fair Value of Warrant Liability

Change in fair value of warrant liability resulted in no expense for the three months ended March 31, 2019, compared to other income of $5,000 for the three months ended March 31, 2018. The preferred stock warrants were subject to remeasurement at each reporting period, with changes in fair value recorded in the condensed statement of operations. The outstanding preferred stock warrants converted into common stock warrants upon the completion of our IPO in October 2018 and, accordingly, we no longer remeasure the fair value of the warrant liability.

Change in Fair Value of Derivative Liability

Change in fair value of derivative liability resulted in no expense for the three months ended March 31, 2019, compared to $0.2 million of expense for the three months ended March 31, 2018. 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 condensed 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 and, accordingly, we no longer remeasure the fair value of the derivative liability.

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 primarily through public offerings of our common stock, private placements of convertible debt and our convertible preferred stock and borrowings under our term loans.

In October 2017, we entered into a loan and security agreement, or SVB Loan, with SVB which provided that we could borrow up to $7.5 million. In March 2019, we entered into a new 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. As of March 31, 2019, we have drawn on one tranche under the 2019 Loan of $7.5 million. The second tranche of $2.5 million, may be drawn through May 31, 2019 and the final tranche of $5.0 million may be drawn upon the achievement of certain clinical milestones related to the development of PB2452.

In August 2018, we received $17.7 million in net proceeds from the sale of our Series D redeemable convertible preferred stock. Concurrent with this financing, all of our outstanding convertible promissory notes, and accrued interest thereon, were converted into 2.1 million shares of Series D redeemable convertible preferred stock.

In October 2018, we completed our IPO of our common stock, which resulted in the issuance and sale of 9.9 million 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. Upon closing of the IPO, all outstanding shares of our redeemable convertible preferred stock were converted into an aggregate of 13.2 million shares of common stock.

As of March 31, 2019, we had cash and cash equivalents of $51.9 million. In April 2019, we completed an underwritten public offering of our common stock, which resulted in the issuance and sale of an aggregate of 4,124,475 shares of common stock at a public offering price of $12.00 per share, generating net proceeds of $46.2 million after deducting underwriting discounts and commissions and other offering costs.

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

	Three Months Ended March 31,	
	2019	2018
Net cash used in operating activities	$ (8,731)	$ (2,634)
Net cash used in investing activities	(84)	(6)
Net cash used in financing activities	(322)	—
Net decrease in cash and cash equivalents	$ (9,137)	$ (2,640)

Operating Activities

Net cash used in operating activities was $8.7 million during the three months ended March 31, 2019. The use of cash primarily related to our net loss of $7.3 million, in addition to a $1.8 million change in our operating assets and liabilities. The change in our operating assets and liabilities was principally due to a $1.5 million decrease in accrued expenses as a result of increased clinical trial payments related to PB2452 in the first quarter of 2019.

Net cash used in operating activities was $2.6 million during the three months ended March 31, 2018. The use of cash primarily related to our net loss of $4.4 million, adjusted for non-cash charges principally related to $1.4 million for non-cash interest expense.

Investing Activities

Net cash used in investing activities was $0.1 million for the purchase of property and equipment during the three months ended March 31, 2019. Net cash used in investing activities was $6,000 for the purchase of property and equipment during the three months ended March 31, 2018.

Financing Activities

Net cash used in financing activities was $0.3 million during the three months ended March 31, 2019, due primarily to repayments of long-term debt of $0.9 million partially offset by borrowings of $0.6 million related to the 2019 Loan. There was no net cash used in or provided by financing activities during the three months ended March 31, 2018.

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 expect our existing cash and cash equivalents as of March 31, 2019, together with the net proceeds from our April 2019 underwritten public offering, are sufficient to fund our operating expenses and capital requirements into the second half of 2020. We intend to devote our existing cash and the net proceeds from the April 2019 offering to advance PB2452 and PB1046, fund the development of our ELP technology and preclinical programs and for general working capital and other general corporate purposes. 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 condensed 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.

Significant estimates include assumptions used in the determination of accrued research and development costs and share-based compensation. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

There were no material changes to our critical accounting policies which are disclosed in our audited financial statements for the years ended December 31, 2018 and 2017 included in our Annual Report on Form 10-K for the year ended December 31, 2018 filed with the SEC on March 26, 2019.

Recent Accounting Pronouncements

See "Note 2. Significant Accounting Policies" in "Notes to Condensed Financial Statements" located in "Part I – Financial Information, Item 1. Financial Statements" in this Quarterly Report on Form 10-Q for information concerning recent accounting pronouncements.

Item 3. Quantitative and Qualitative Disclosures About Market Risks

Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our cash equivalents are in the form of a money market fund and marketable securities and are invested in U.S. Treasury obligations. A hypothetical 1% increase in interest rates as of March 31, 2019 and December 31, 2018 would have resulted in immaterial decreases in the fair values of our cash equivalents at those dates. We do not currently use interest rate derivative instruments to manage exposure to interest rate changes.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the three months ended March 31, 2019 or year ended December 31, 2018

Item 4. 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 Chief Executive Officer and our Chief Financial Officer, to allow timely decisions regarding required disclosure.

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.

With respect to the quarter ended March 31, 2019, 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 are effective.

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. Because of the inherent limitations in a cost-effective control system, no evaluation of internal control over financial reporting can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud, if any, have been or will be detected.

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 quarter ended March 31, 2019 which have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

Item 1. 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 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 Quarterly Report on Form 10-Q 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 Quarterly Report on Form 10-Q 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 $7.3 million for the quarter ended March 31, 2019. As of March 31, 2019, we had an accumulated deficit of $130.2 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 have initiated a Phase 2a trial of PB2452 and 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.

As of March 31, 2019, we had cash and cash equivalents of $51.9 million. In April 2019, we received $46.2 million in aggregate net proceeds from an underwritten public offering of our common stock. We believe that our existing cash and cash equivalents as of March 31, 2019, together with the net proceeds from our April 2019 offering, are sufficient to fund our operating expenses and capital requirements into the second half 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 the 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 PB2452, or any other 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 have received a Breakthrough Therapy designation for PB2452 for the reversal of ticagrelor's antiplatelet activity and may, in the future, apply for Breakthrough Therapy designation for other 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 PB2452, or any other 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, the FDA may later decide that PB2452, or any product candidate that may receive Breakthrough Therapy designation, 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 $P2Y_{12}$ 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 $P2Y_{12}$ 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, which we have licensed 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 March 31, 2019, 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, marketing expenditures or drug pricing; 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, 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. However, companies may share truthful and not misleading information that is not inconsistent with the labeling. 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 that repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." 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, amended 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, or HHS, has already started the process of soliciting feedback on some of these measures and, at the same, is immediately implementing others under its existing authority. For example, in September 2018, 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. Further, on January 31, 2019, the HHS Office of Inspector General

proposed modifications to federal Anti-Kickback Statute safe harbors which, among other things, may affect rebates paid by manufacturers to Medicare Part D plans, the purpose of which is to further reduce the cost of drug products to consumers. Although a number of these and other proposed measures will require additional authorization 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 March 31, 2019, we had 27 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, 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 has been, and may continue to be, volatile. Since our IPO, our common stock has traded at prices ranging from $2.55 to $16.65 per share. 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 available for immediate resale, and the remainder will be eligible to 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.

Following the expiration in April of the lockup agreements between the pre-IPO holders of substantially all of our outstanding stock, the vast majority of our outstanding shares of common stock are available for immediate resale in the public market, with the exception of approximately 10 million shares that are subject to lockup agreements with the underwriters for our recent follow-on offering, which agreements expire 60 calendar days following the pricing of the follow-on offering. 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.

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 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 ⅔% 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 have broad discretion in the use of our cash and cash equivalents.

We have broad discretion over the use of our cash and cash equivalents, including the net proceeds from our recent public offerings. 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 have begun incurring 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 2. Recent Sales of Unregistered Securities and Use of Proceeds

(b) Use of Proceeds

On October 17, 2018, our Registration Statement on Form S-1, as amended (File No. 333-227474), was declared effective in connection with our IPO, pursuant to which we sold an aggregate of 9,864,666 shares of our common stock, including the partial exercise of the underwriters' option to purchase additional shares, at a price to the public 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 IPO closed on October 22, 2018 with respect to 9,200,000 shares of common stock. 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 IPO, 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 as described in our prospectus filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on October 19, 2018.

Item 3. Defaults Upon Senior Securities

Not applicable.

Item 4. Mine Safety Disclosures

Not applicable.

Item 5. Other Information

Not applicable.

Item 6. Exhibits

The exhibits listed on the Exhibit Index are either filed or furnished with this report or incorporated herein by reference.

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.	10-K	001-38697	4.4	March 26, 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-K	001-38697	4.5	March 26, 2019
10.1	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-K	001-38697	10.13	March 26, 2019
10.2†	Master Services Agreement, dated as of November 14, 2018, by and between PhaseBio Pharmaceuticals, Inc. and BioVectra Inc.	10-K	001-38697	10.14	March 26, 2019
10.3+	Non-Employee Director Compensation Policy, as amended.	8-K	001-38697	10.1	March 4, 2019
10.4†	Eighth Amendment to License Agreement, dated as of March 5, 2019, by and between PhaseBio Pharmaceuticals, Inc. and Duke University	8-K	001-38697	10.1	April 9, 2019
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.				

† 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.

+ Indicates management contract or compensatory plan.

Filed herewith.

* 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.

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.

May 9, 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*)

Exhibit 31.1

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 Quarterly Report on Form 10-Q 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: May 9, 2019

By: /s/ Jonathan P. Mow
Jonathan P. Mow
Chief Executive Officer

Exhibit 31.2

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 Quarterly Report on Form 10-Q 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: May 9, 2019

By: /s/ John Sharp
John Sharp
Chief Financial Officer

Exhibit 32.1

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 Quarterly Report of PhaseBio Pharmaceuticals, Inc. ("the Company") on Form 10-Q for the period ending March 31, 2019 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: May 9, 2019

By: /s/ Jonathan P. Mow
Jonathan P. Mow
Chief Executive Officer

Exhibit 32.2

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 Quarterly Report of PhaseBio Pharmaceuticals, Inc. (the "Company") on Form 10-Q for the period ending March 31, 2019 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: May 9, 2019

By: /s/ John Sharp
John Sharp
Chief Financial Officer