SUBJECT TO COMPLETION, DATED OCTOBER 5, 2018

**PRELIMINARY PROSPECTUS**

# 5,000,000 Shares

# PHASE Bio

# Common Stock

This is the initial public offering of our common stock. We are selling 5,000,000 shares of our common stock. We currently expect that the initial public offering price will be between $12.00 and $14.00 per share of common stock.

We have granted the underwriters an option to purchase up to an additional 750,000 shares of common stock to cover over-allotments, if any.

We have applied to list our common stock on the Nasdaq Global Market under the symbol "PHAS."

**Investing in our common stock involves a high degree of risk. See "Risk Factors" beginning on page 10.**

We are an "emerging growth company" as defined under the U.S. federal securities laws and, as such, may elect to comply with certain reduced public company reporting requirements for this and future filings.

**Neither the Securities and Exchange Commission nor any state securities regulators have approved or disapproved of these securities, or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.**

| | Per Share | Total |
|---|---|---|
| Public offering price | $ | $ |
| Underwriting discounts and commissions[(1)] | $ | $ |
| Proceeds to PhaseBio Pharmaceuticals, Inc. (before expenses) | $ | $ |

(1) We refer you to "Underwriting" beginning on page 156 for additional information regarding underwriting compensation.

Certain of our existing stockholders, including entities affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of approximately $25.0 million in shares of our common stock in this offering at the initial public offering price per share. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any of these persons or entities, or any of these persons or entities may determine to purchase more, less or no shares in this offering. The underwriters will receive the same underwriting discount on any shares purchased by these persons or entities as they will on any other shares sold to the public in this offering.

The underwriters expect to deliver the shares to purchasers against payment in New York, New York on or about , 2018 through the book-entry facilities of The Depositary Trust Company.

**Citigroup** **Cowen** **Stifel**

**Needham & Company**

, 2018

**You should rely only on the information contained in this prospectus and any free writing prospectus prepared by or on behalf of us or to which we have referred you. We have not authorized anyone to provide you with different information, and we take no responsibility for any other information others may give you. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained in this prospectus is accurate as of any date other than the date on the front of this prospectus.**

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For investors outside the United States: We and the underwriters have not done anything that would permit this offering or the possession or distribution of this prospectus in any jurisdiction where action for those purposes is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside of the United States.

This prospectus contains trade names, trademarks and service marks of others, which are the property of their respective owners. Solely for convenience, trademarks and trade names referred to in this prospectus may appear without the ® or TM symbols.

## PROSPECTUS SUMMARY

*This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our financial statements and the related notes and the information set forth under the sections titled "Risk Factors," "Special Note Regarding Forward-Looking Statements" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," in each case included elsewhere in this prospectus. Unless the context otherwise requires, we use the terms "PhaseBio," "company," "our," "us" and "we" in this prospectus to refer to PhaseBio Pharmaceuticals, Inc.*

### Overview

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

PB2452 is a novel recombinant human monoclonal antibody antigen-binding fragment, or Fab fragment, designed to reverse the antiplatelet activity of ticagrelor. Ticagrelor is an antiplatelet therapy widely prescribed to reduce the rates of death, heart attack and stroke in patients with acute coronary syndrome, or ACS, or who have previously experienced a heart attack. The American College of Cardiology, American Heart Association and European Society of Cardiology guidelines recognize ticagrelor as the preferred antiplatelet therapy for ACS. In 2017, ticagrelor, currently marketed by AstraZeneca plc, or AstraZeneca, under the brand names Brilinta and Brilique, had worldwide sales of over $1 billion, an increase of 29% over 2016 sales. In the first half of 2018, ticagrelor had worldwide sales of $609 million, an increase of 23% over sales in the first half of 2017. Ticagrelor binds to platelets to prevent them from forming blood clots, which could restrict blood flow to critical organs in these patients, causing heart attacks or strokes. Due to ticagrelor's antiplatelet activity, patients on ticagrelor have an elevated risk of spontaneous bleeding. In addition, patients on ticagrelor who need urgent surgery cannot wait the recommended five days for ticagrelor's effect to dissipate and are at increased risk of major bleeding during and after surgery. There are currently no known reversal agents approved or in clinical development for ticagrelor or any of the other antiplatelet drugs. In our Phase 1 clinical trial, PB2452 achieved rapid and complete reversal of ticagrelor's antiplatelet activity, with potential customizable duration of reversal based on the dosing regimen, which we believe has the potential to bring life-saving therapeutic benefit to these patients by increasing the safety of ticagrelor. We believe the availability of a reversal agent could expand ticagrelor's use by mitigating concerns regarding bleeding risk and uniquely position ticagrelor as the only oral antiplatelet drug with a reversal agent.

We recently completed a Phase 1 dose escalation clinical trial of PB2452 in healthy subjects ages 18 to 50 who had been pre-dosed with ticagrelor. In this trial, we observed rapid and complete reversal of ticagrelor's antiplatelet activity within five minutes following initiation of infusion, and sustained reversal for over 20 hours, in later dosing cohorts in which we administered PB2452 over an extended infusion period. Based on our observations in our Phase 1 trial, duration of reversal may be controlled by duration of the infusion, which may allow for customization based on patient needs. There were no PB2452-related adverse events or serious adverse events, or SAEs, in any of the dose cohorts. We believe that the results of the Phase 1 trial support the continued development of PB2452 to treat ticagrelor patients who are experiencing a major bleeding event or those who require urgent surgery.

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

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

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

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

PB1046 and our preclinical product candidates are based on our proprietary ELP technology. Our ELP technology extends the circulating half-life of proteins and peptides and also provides a sustained-release mechanism, resulting in exposure of active molecules for periods of a week or longer from a single subcutaneous injection. We believe that our ELP technology enhances solubility, stability and bioavailability, provides extended drug exposure and creates product candidates that are straightforward to manufacture and administer.

Our strategy is to apply our ELP technology to proteins and peptides with well-characterized therapeutic activities but suboptimal half-lives to improve their pharmacokinetics, enable their use as pharmaceutical products and allow for more convenient dosing regimens. To date, we have not observed any drug-related SAEs in any of the over 500 subjects in clinical trials of our ELP product candidates.

We have an experienced management team that includes individuals with experience in translational research, orphan and cardiopulmonary drug discovery, development and commercialization. We are led by our Chief Executive Officer, Jonathan P. Mow, who brings more than 25 years of experience in biotechnology management, including previous executive experience at Amylin Pharmaceuticals, Corus Pharma, PathoGenesis and Bristol-Myers Squibb. We have been supported by a leading group of biotechnology investors, including funds and accounts managed by New Enterprise Associates, Hatteras Venture Partners, Johnson & Johnson Innovation — JJDC, Inc., Fletcher Spaght Ventures, Syno Capital, Astellas Venture Management, Cormorant Asset Management, Rock Springs Capital and Mountain Group Partners, as well as AstraZeneca, from whom we licensed PB2452.

**Strategy**

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

- ***Continue to advance PB2452 through clinical development and regulatory approval***. We intend to develop and commercialize PB2452 as a novel reversal agent for the antiplatelet drug ticagrelor. If considered appropriate by the FDA, we intend to pursue accelerated approval, which would allow us to submit a BLA prior to completion of the Phase 3 clinical trial based on biomarker data from an initial subset of the Phase 3 patients.

- ***Continue to develop PB1046***. We intend to advance PB1046 through clinical trials as a once-weekly novel treatment for PAH that is vasodilatory, potentially disease-modifying and complementary to the current standard of care therapies. We are currently conducting a Phase 2b clinical trial of PB1046 and expect to report results from this trial in the first half of 2020. Based on the results of this trial, we intend to advance this product candidate into Phase 3 clinical development for the treatment of PAH.

- ***Broaden the potential therapeutic applications of PB1046***. We believe that the therapeutic potential of VIP can be applied to a variety of other orphan indications. As such, we intend to strategically broaden the therapeutic applications of PB1046 by exploring its development in additional indications, including cardiomyopathy associated with Duchenne Muscular Dystrophy, or DMD, heart failure and other cardiomyopathies and cystic fibrosis.

- ***Leverage our ELP technology platform to expand our development pipeline***. We intend to apply our ELP technology to improve the pharmacokinetics of proteins and peptides with well-characterized therapeutic activities but suboptimal half-lives, in order to improve their pharmacokinetics, enable their use as pharmaceutical products and allow for more convenient dosing regimens in additional orphan indications.

- ***Commercialize our product candidates***. We have entered into exclusive license agreements with AstraZeneca for PB2452 and Duke University for our ELP technology, pursuant to which we retain worldwide commercial rights to our product candidates. If approved in the United States, we intend to commercialize PB2452 independently and we may either commercialize PB1046 independently or in collaboration with a partner. As we advance towards regulatory approvals for our product candidates, we intend to establish a focused marketing and sales infrastructure. We may also explore collaborations or partnerships to commercialize PB2452 and PB1046 outside of the United States.

**Pipeline**

Our clinical-stage pipeline is set forth below:

| Product Candidate | Indication | Mechanism of Action | Stage of Development | Worldwide Commercial Rights | Upcoming Milestones |
|---|---|---|---|---|---|
| PB2452 | Major Bleeding or Prior to Urgent Surgery in Patients on Ticagrelor | Reversal of the Antiplatelet Activity of Ticagrelor | **Phase 1** | PHASE Bio | **YE2018:** Phase 1 Full Data **1H2019:** Initiate Phase 2a and Report Data **2H2019:** Initiate Phase 2 Trial |
| PB1046 | Pulmonary Arterial Hypertension | VPAC2 Selective Agonist | **Phase 2b** | PHASE Bio | **1H2020:** Phase 2b Data |

**Risks Associated with Our Business**

Our business is subject to a number of risks of which you should be aware before making a decision to invest in our common stock. These risks are more fully described in the section titled "Risk Factors," including the following:

- 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.
- Our management and our independent registered public accounting firm have expressed substantial doubt about our ability to continue as a going concern.
- Even if this offering is successful, 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.
- 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.
- If considered appropriate by the FDA, we intend to seek regulatory approval of PB2452 in the United States through an accelerated approval process with the FDA. If we are not successful with this process, the development or commercialization of PB2452 could be delayed, abandoned or significantly more costly.
- 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.
- Market acceptance of PB2452, if approved, will depend heavily on the continued market acceptance and use of ticagrelor.
- We contract with third parties for the manufacture of PB2452 and PB1046 for preclinical and clinical testing and expect to continue to do so for commercialization. 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.

- 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.
- 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.

**Corporate Information**

We were incorporated under the laws of the State of Delaware in January 2002. Our principal executive offices are located at 1 Great Valley Parkway, Suite 30, Malvern, Pennsylvania 19355. Our telephone number is (610) 981-6500. Our website address is *www.phasebio.com*. We have included our website address in this prospectus solely as an inactive textual reference.

**Implications of Being an Emerging Growth Company**

We qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. An emerging growth company may take advantage of specified reduced reporting and other burdens that are otherwise applicable generally to public companies. These provisions include:

- a requirement to have only two years of audited financial statements and only two years of related selected financial data and management's discussion and analysis of financial condition and results of operations disclosure;
- an exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting pursuant to the Sarbanes-Oxley Act of 2002;
- an exemption from implementation of new or revised financial accounting standards until they would apply to private companies and from compliance with any new requirements adopted by the Public Company Accounting Oversight Board requiring mandatory audit firm rotation;
- reduced disclosure obligations regarding executive compensation arrangements; and
- no requirement to seek nonbinding advisory votes on executive compensation or golden parachute arrangements.

We may take advantage of some or all these provisions until we are no longer an emerging growth company. We will remain an emerging growth company until the earlier to occur of (1) the last day of the fiscal year (a) following the fifth anniversary of the closing of this offering, (b) in which we have total annual gross revenues of at least $1.07 billion or (c) in which we are deemed to be a "large accelerated filer," under the rules of the U.S. Securities and Exchange Commission which means the market value of our equity securities 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.

**THE OFFERING**

| | |
|---|---|
| Common stock to be offered | 5,000,000 shares |
| Common stock to be outstanding after this offering | 19,588,404 shares |
| Over-allotment option | 750,000 shares |
| Use of proceeds | We estimate that the net proceeds from this offering will be approximately $57.9 million (or approximately $67.0 million if the underwriters exercise in full their option to purchase up to 750,000 additional shares of common stock to cover over-allotments, if any), based on an assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriter discounts and commissions and estimated offering expenses payable by us.<br><br>We intend to use the net proceeds from this offering, together with our existing cash, to advance PB2452, advance PB1046, fund the development of our ELP technology and preclinical programs and for general working capital and other general corporate purposes. These expectations are subject to change. See "Use of Proceeds" for additional information. |
| Risk factors | See "Risk Factors" and the other information included in this prospectus for a discussion of factors you should carefully consider before deciding to invest in our common stock. |
| Proposed Nasdaq Global Market symbol | "PHAS" |

The number of shares of our common stock that will be outstanding after this offering is based on 14,588,404 shares of common stock outstanding as of June 30, 2018, which gives effect to (1) the automatic conversion of all outstanding shares of our redeemable convertible preferred stock into 13,064,781 shares of common stock and (2) the expected exercise of warrants to purchase 777,835 shares of our redeemable convertible preferred stock, at a weighted-average exercise price of $0.12 per share, and the automatic conversion thereof into 777,835 shares of common stock as of June 30, 2018, and excludes:

- 1,210,776 shares of common stock issuable upon the exercise of options outstanding as of June 30, 2018, at a weighted-average exercise price of $1.68 per share;
- 90,256 shares of common stock reserved for future issuance under our Amended and Restated 2002 Stock Plan, or the 2002 Plan, as of June 30, 2018, which shares will cease to be available for issuance at the time our 2018 Equity Incentive Plan becomes effective;
- 75,597 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2018, at a weighted-average exercise price of $9.659 per share, which warrants are expected to remain outstanding following the closing of this offering;

- 1,878,041 shares of common stock reserved for future issuance under our 2018 Equity Incentive Plan, or the 2018 Plan, which will become effective in connection with this offering; and
- 196,000 shares of common stock reserved for future issuance pursuant to our 2018 Employee Stock Purchase Plan, which will become effective prior to the closing of this offering.

Unless otherwise indicated, this prospectus reflects and assumes the following:

- the automatic conversion of all outstanding shares of our Series 1 redeemable convertible preferred stock, Series AA redeemable convertible preferred stock, Series B redeemable convertible preferred stock, Series C-1 redeemable convertible preferred stock and Series D redeemable convertible preferred stock into an aggregate of 13,055,166 shares of our common stock immediately prior to the closing of this offering;
- the automatic conversion of the outstanding share of our Series 2 redeemable convertible preferred stock into an aggregate of 9,615 shares of our common stock, based on an assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus;
- the exercise of outstanding warrants to purchase 777,835 shares of our redeemable convertible preferred stock, and the automatic conversion thereof into 777,835 shares of common stock, which we expect will occur immediately prior to the closing of this offering;
- the conversion of outstanding warrants to purchase 75,597 shares of our redeemable convertible preferred stock into warrants to purchase 75,597 shares of our common stock immediately prior to the closing of this offering;
- no exercise of any other outstanding options or warrants after June 30, 2018;
- no exercise by the underwriters of their option to purchase up to 750,000 additional shares of our common stock to cover over-allotments, if any;
- a 11.0634-for-1 reverse stock split of our common and redeemable convertible preferred stock effected on October 4, 2018; and
- the filing and effectiveness of our amended and restated certificate of incorporation in Delaware and the adoption of our amended and restated bylaws, each of which will occur immediately prior to the closing of this offering.

Certain of our existing stockholders, including entities affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of approximately $25.0 million in shares of our common stock in this offering at the initial public offering price per share. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any of these persons or entities, or any of these persons or entities may determine to purchase more, less or no shares in this offering. The underwriters will receive the same underwriting discount on any shares purchased by these persons or entities as they will on any other shares sold to the public in this offering.

## SUMMARY FINANCIAL DATA

You should read the following summary financial data together with our financial statements and the related notes thereto appearing at the end of this prospectus and the "Selected Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of this prospectus. We have derived the statements of operations data for the years ended December 31, 2016 and 2017 from our audited financial statements appearing at the end of this prospectus. The statements of operations data for the six months ended June 30, 2017 and 2018 and the balance sheet data as of June 30, 2018 have been derived from our unaudited interim financial statements appearing at the end of this prospectus and have been prepared on the same basis as the audited financial statements. In the opinion of management, the unaudited data reflects all adjustments, consisting only of normal recurring adjustments, considered necessary for a fair presentation of the financial information in those statements. Our historical results are not necessarily indicative of the results that should be expected in the future and the results for the six months ended June 30, 2018 are not necessarily indicative of the results to be expected for the full year ending December 31, 2018 or any other future period.

| | Year Ended December 31, | | Six Months Ended June 30, | |
|---|---|---|---|---|
| | 2016 | 2017 | 2017 | 2018 |
| | (in thousands, except share and per share data) | | (unaudited) | |
| **Statements of Operations Data:** | | | | |
| Operating expenses: | | | | |
| Research and development | $ 7,376 | $ 6,210 | $ 3,057 | $ 5,425 |
| General and administrative | 2,125 | 2,328 | 1,135 | 1,560 |
| Total operating expenses | 9,501 | 8,538 | 4,192 | 6,985 |
| Loss from operations | (9,501) | (8,538) | (4,192) | (6,985) |
| Other income (expense): | | | | |
| Interest income | 29 | 52 | 15 | 72 |
| Interest expense | — | (2,723) | (987) | (2,851) |
| Change in fair value of warrant liability | 252 | 1,019 | 125 | (996) |
| Change in fair value of derivative liability | — | (57) | (113) | (317) |
| Total other income (expense) | 281 | (1,709) | (960) | (4,092) |
| Net loss | (9,220) | (10,247) | (5,152) | (11,077) |
| Net loss per common share, basic and diluted[(1)] | $ (12.41) | $ (13.78) | $ (6.93) | $ (14.85) |
| Weighted-average common shares outstanding, basic and diluted[(1)] | 742,808 | 743,470 | 743,241 | 745,788 |
| Pro forma net loss per common share, basic and diluted (unaudited)[(1)] | | $ (0.76) | | $ (0.58) |
| Pro forma weighted-average common shares outstanding, basic and diluted (unaudited)[(1)] | | 11,235,815 | | 12,376,871 |

(1) See Note 2 to our financial statements appearing at the end of this prospectus for an explanation of the method used to calculate the historical and pro forma net loss per common share, basic and diluted.

The following table presents our summary balance sheet data as of June 30, 2018:

- on an actual basis;
- on a pro forma basis to give effect to (1) the automatic conversion of all outstanding shares of our redeemable convertible preferred stock into an aggregate of 13,064,781 shares of common stock, including

the conversion of 3,923,168 shares of Series D redeemable convertible preferred stock that we issued in August 2018, based on an assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus; (2) the expected exercise of outstanding warrants to purchase 777,835 shares of our redeemable convertible preferred stock, including warrants to purchase 368,582 shares of Series C-1 redeemable convertible preferred stock that we issued in August 2018 in conjunction with the issuance of our Series D redeemable convertible preferred stock, and the automatic conversion thereof into 777,835 shares of common stock, which will occur immediately prior to the closing of this offering; (3) the receipt of $17.7 million in net proceeds from our sale of Series D redeemable convertible preferred stock; (4) the conversion of our outstanding convertible promissory notes, and accrued interest thereon; and (5) the receipt of $2.0 million in additional borrowings under the loan and security agreement with Silicon Valley Bank, as if such events had occurred on June 30, 2018; and

- on a pro forma as adjusted basis to give further effect to our issuance and sale of 5,000,000 shares of common stock in this offering at an assumed initial public offering price of $13.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discounts and estimated offering expenses payable by us.

| | As of June 30, 2018 | | |
|---|---|---|---|
| | Actual | Pro Forma | Pro Forma As Adjusted |
| | | (in thousands) | |
| **Balance Sheet Data:** | | (unaudited) | |
| Cash and cash equivalents | $ 8,734 | 28,446 | 86,352 |
| Working capital (deficit)[(1)] | (14,348) | 23,547 | 82,057 |
| Total assets | 9,889 | 29,601 | 86,897 |
| Convertible promissory notes | 14,140 | — | — |
| Long-term debt, including current portion | 5,490 | 7,490 | 7,490 |
| Redeemable convertible preferred stock | 89,667 | — | — |
| Total stockholders' (deficit) equity | (108,360) | 20,354 | 78,254 |

(1) We define working capital (deficit) as total current assets less total current liabilities. See our financial statements appearing at the end of this prospectus for further details regarding our current assets and current liabilities.

The pro forma as adjusted data discussed above is illustrative only and will be adjusted based on the actual initial public offering price and other terms of our initial public offering determined at pricing. Each $1.00 increase (decrease) in the assumed initial public offering price of $13.00 per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, working capital (deficit), total assets, and total stockholders' (deficit) equity by $4.7 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase (decrease) of 1.0 million shares in the number of shares offered by us at the assumed initial public offering price would increase (decrease) each of cash and cash equivalents, working capital (deficit), total assets, and total stockholders' (deficit) equity by $12.1 million.

## RISK FACTORS

*Investing in our common stock involves a high degree of risk. You should consider carefully the risks and uncertainties described below, together with all of the other information in this prospectus, including our financial statements and related notes, before deciding whether to purchase shares of our common stock. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties that we are unaware of, or that we currently believe are not material, may also become important factors that affect us. If any of the following risks are realized, our business, financial condition, results of operations and prospects could be materially and adversely affected. In that event, the price of our common stock could decline, and you could lose part or all of your investment.*

### 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 inception, we have incurred significant net losses. We incurred net losses of $9.2 million and $10.2 million for the years ended December 31, 2016 and 2017, respectively, and $11.1 million for the six months ended June 30, 2018. As of June 30, 2018, we had an accumulated deficit of $110.1 million. Since inception, we have financed our operations with $121.7 million in gross proceeds raised in private placements of convertible debt and convertible preferred stock. We have no products approved for commercialization and have never generated any revenue.

We have devoted substantially all of our financial resources and efforts to the development of our clinical and preclinical product candidates and our proprietary half-life extending elastin-like polypeptide, or ELP, technology, including conducting preclinical studies and clinical trials. We recently completed a Phase 1 clinical trial of PB2452 and 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.

***Our management and our independent registered public accounting firm have expressed substantial doubt about our ability to continue as a going concern.***

Our management has concluded that our need for additional funding raises substantial doubt about our ability to continue as a going concern. In addition, as described in their audit report, our auditors have included an explanatory paragraph that states we have incurred recurring losses and negative cash flows from operations that raise substantial doubt about our ability to continue as a going concern. Our financial statements do not include any adjustments that might result from the outcome of this uncertainty. If we cannot continue as a viable entity, our stockholders may lose some or all of their investment in us.

***We have a limited operating history and no history of commercializing products, which may make it difficult for you 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.

***Even if this offering is successful, 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 June 30, 2018, we had cash and cash equivalents of $8.7 million. In August 2018, we received $17.7 million in net proceeds from the sale of our Series D redeemable convertible preferred stock and we received $2.0 million in additional borrowings under our loan and security agreement with Silicon Valley Bank. We believe that the anticipated net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements into the third quarter of 2020. This estimate is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we expect. Changes may occur beyond our control that would cause us to consume our available capital before that time, including changes in and progress of our development activities, acquisitions of additional product candidates, and changes in regulation. Our future capital requirements will depend on many factors, including:

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

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

***Raising additional capital may cause dilution to our stockholders, including purchasers of common stock in this offering, 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, debt financings and license and collaboration agreements. 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 Silicon Valley Bank, or SVB, 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 may preclude future debt financing or make the terms of such financings less favorable.

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

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

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

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

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

- timely and successful completion of preclinical studies and our clinical trials;
- sufficiency of our financial and other resources to complete the necessary preclinical studies and clinical trials;
- successful enrollment and completion of clinical trials;
- successful development of, or making arrangements with third-party manufacturers for, our commercial manufacturing processes for any of our product candidates that receive regulatory approval;
- receipt of timely marketing approvals from applicable regulatory authorities;
- launching commercial sales of products, if approved;
- acceptance of our products, if approved, by patients, the medical community and third-party payors, for their approved indications;
- the prevalence and severity of adverse events experienced with PB2452, PB1046 or any other product candidates;

- the availability, perceived advantages, cost, safety and efficacy of alternative therapies for any product candidate, and any indications for such product candidate, that we develop, specifically, alternative antiplatelet therapies to ticagrelor, including therapies that may be developed with a reversal agent, alternative reversal agents for ticagrelor or alternative treatments for PAH;
- our ability to produce PB2452, PB1046 or any other product candidates we develop on a commercial scale;
- obtaining and maintaining patent, trademark and trade secret protection and regulatory exclusivity for our product candidates and otherwise protecting our rights in our intellectual property portfolio;
- maintaining compliance with regulatory requirements, including current good manufacturing practices, or cGMPs;
- competing effectively with other procedures; and
- maintaining a continued acceptable safety, tolerability and efficacy profile of the products following approval.

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

***The regulatory approval processes of the 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 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 program.

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 biologics license application, or 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 that 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 with the FDA. 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, and our BLA would be based on biomarker data from an initial subset of patients. 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 results. 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 candidates, we may not obtain orphan exclusivity and that exclusivity may not effectively protect the drug from the competition of different drugs for the same condition, which could be approved during the exclusivity period. Additionally, after an orphan drug is approved, the FDA could subsequently approve another application for the same drug for the same indication if the FDA concludes that the later drug is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusive marketing rights in the United States also may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. The failure to obtain an orphan drug designation for any product candidates we may develop, the inability to maintain that designation for the duration of the applicable period, or the inability to obtain or maintain orphan drug exclusivity could reduce our ability to make sufficient sales of the applicable product candidate to balance our expenses incurred to develop it, which would have a negative impact on our operational results and financial condition.

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

We may seek a breakthrough therapy designation for one or more product candidates. A breakthrough therapy is defined as a product candidate that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For product

candidates that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Product candidates designated as breakthrough therapies by the FDA are also eligible for priority review if supported by clinical data at the time of the submission of the BLA.

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

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

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

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

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

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

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

The commercial success of PB2452 as a ticagrelor reversal agent, if approved, is dependent on the continued market acceptance and use of ticagrelor as an antiplatelet therapy. Ticagrelor competes against other commercially available antiplatelet therapies, including other $P2Y_{12}$ 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 receives 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 receives marketing approval, it 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.

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 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 or PB1046, 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 is made on a payor-by-payor basis. One payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage, and adequate reimbursement.

Third-party payors determine which 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 or PB1046, if approved for sale in the United States or in other countries, will be considered medically reasonable and necessary, that they 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, fails 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 preclinical and clinical testing and expect to continue to do so for commercialization. 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 or personnel. 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 preclinical and clinical testing as well as for commercial manufacture of PB2452, PB1046 or any other product candidate which we may pursue receives marketing approval. We also rely on a proprietary third-party strain of *E. coli* owned by Wacker Biotech GmbH, or Wacker, for the production of PB2452. Our reliance on Wacker's *E. coli* strain increases the risk that we will not have sufficient quantities of PB2452 or be able to obtain quantities at an acceptable cost or quality, which could delay, prevent or impair our ability to timely conduct our clinical trials or our other development or commercialization efforts.

With respect to PB2452, to date, we have used PB2452 provided to us pursuant to our license agreement for our Phase 1 clinical trial, which was manufactured by Wacker. Wacker is currently developing, and scaling up, a more efficient manufacturing process for PB2452, which we expect to use to manufacture future clinical and, if PB2452 is approved, commercial supply. We will need to perform analytical and other tests to demonstrate that the new materials produced by Wacker, or any other future third-party manufacturer that we engage, are comparable in all respects, including potency, 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 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. Although Wacker's manufacturing capacity has been sufficient for our early clinical needs, Wacker 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 Wacker is unable to successfully scale up its manufacturing process, we would need to find alternative manufacturing facilities, 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 outside the United States 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 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. 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 September 30, 2018, 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, 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, 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 its implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information on health plans, healthcare clearinghouses and certain healthcare providers, known as "covered entities", and their respective HIPAA "business associates", independent contractors that perform certain services involving the use or disclosure of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorneys' fees and costs associated with pursuing federal civil actions;

- the federal transparency laws, including the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, medical devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the State Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to: (1) payments or other "transfers of value'' made to physicians and teaching hospitals, and (2) ownership and investment interests held by physicians and their immediate family members; and

- state and foreign law equivalents of each of the above federal laws and regulations; state laws that require manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or that otherwise restrict payments that may be made to healthcare providers; state and local laws that require the registration of pharmaceutical sales representatives; and state and foreign laws that govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant penalties, including, without limitation, civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from participating in federal and state funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, diminished profits and future earnings, reputational harm and the curtailment or restructuring of our operations, any of which could harm our business.

The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to

build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance and/or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

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

Even if we obtain any regulatory approval for PB2452, PB1046 or any future product candidates, such product candidates, once approved, will be subject to ongoing regulatory requirements applicable to manufacturing, labeling, packaging, storage, advertising, promoting, sampling, record-keeping and submitting of safety and other post-market information, among other things. Any regulatory approvals that we receive for PB2452, PB1046 or any future product candidates may also be subject to a risk evaluation and mitigation strategy, limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or requirements that we conduct potentially costly post-marketing testing, including Phase 4 trials, and in the event that we receive accelerated approval of PB2452, the completion of our 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. 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 agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; (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 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget

Act of 2018, or the BBA, among other things, amends the ACA, effective January 1, 2019, to increase from 50% to 70% the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." We continue to evaluate the potential impact of the ACA and its possible repeal or replacement on our business. More recently, in July 2018, CMS announced that it is suspending further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program pending the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment.

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

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

More recently, 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. We have not entered into employment agreements with any of our executive officers, and each of them 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 September 30, 2018, we had 18 full-time employees. As our development progresses, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of clinical product development, regulatory affairs and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

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

We are exposed to the risk that our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, suppliers and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates FDA regulations, including those laws requiring the reporting of true, complete and accurate information to the FDA, manufacturing standards, federal and state healthcare laws and regulations, and laws that require the true, complete and accurate reporting of financial information or data. In particular, sales, marketing and business arrangements in the healthcare industry are

subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct by these parties could also involve the improper use of individually identifiable information, including, without limitation, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, including, without limitation, damages, fines, disgorgement, individual imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations.

**Risks Related to this Offering, Ownership of Our Common Stock and Our Status as a Public Company**

***An active trading market for our common stock may not develop and you may not be able to resell your shares of our common stock at or above the initial offering price, if at all.***

Prior to this offering, there has been no public market for our common stock. The initial public offering price for our common stock will be determined through negotiations with the underwriters and may not be indicative of the price at which our common stock will trade after the closing of this offering. Although we have applied to list our common stock on The Nasdaq Global Market, an active trading market for our shares may never develop or be sustained following this offering. If an active market for our common stock does not develop or is not sustained, it may be difficult for you to sell shares you purchased in this offering at an attractive price or at all.

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

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

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

- conditions or trends in our industry;
- changes in the market valuations of similar companies;
- stock market price and volume fluctuations of comparable companies and, in particular, those that operate in the biopharmaceutical industry;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- announcements by us or our competitors of significant acquisitions, strategic partnerships or divestitures;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- investors' general perception of our company and our business;
- recruitment or departure of key personnel;
- overall performance of the equity markets;
- trading volume of our common stock;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation;
- 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. We do not currently have and may never obtain research coverage by equity research analysts. Equity research analysts may elect not to provide research coverage of our common stock after this offering, 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.

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

The initial public offering price of our common stock is substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our pro forma as adjusted net tangible book value per share after

this offering. Based on the assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, you will experience immediate dilution of $9.01 per share, representing the difference between our pro forma as adjusted net tangible book value per share after this offering and the assumed initial public offering price.

In addition, as of June 30, 2018, we had outstanding stock options to purchase an aggregate of 1,210,776 shares of common stock at a weighted average exercise price of $1.68 per share. To the extent these outstanding options are exercised, there will be further dilution to investors in this offering.

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

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

Upon the closing of this offering, we will have outstanding 19,588,404 shares of common stock, after giving effect to (1) the automatic conversion of our redeemable convertible preferred stock outstanding as of June 30, 2018, including the Series D redeemable convertible preferred stock that we issued in August 2018, into 13,064,781 shares of our common stock and (2) the expected exercise of outstanding warrants to purchase 777,835 shares of our redeemable convertible preferred stock, and the automatic conversion thereof into 777,835 shares of common stock, and assuming no exercise of outstanding options or other outstanding warrants to purchase shares of our redeemable convertible preferred stock. Of these shares, the 5,000,000 shares sold in this offering will be freely tradable and substantially all of the 14,588,404 additional shares of common stock will be available for sale in the public market beginning 180 days after the date of this prospectus following the expiration of lock-up agreements between some of our stockholders and the underwriters. Citigroup Global Markets Inc. and Cowen and Company, LLC may release these stockholders from their lock-up agreements with the underwriters at any time and without notice, which would allow for earlier sales of shares in the public market.

In addition, promptly following the closing of this offering, we intend to file one or more registration statements on Form S-8 under the Securities Act of 1933, as amended, or the Securities Act, registering the issuance of 3,427,626 shares of common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. Shares registered under these registration statements on Form S-8 will be available for sale in the public market subject to vesting arrangements and exercise of options, the lock-up agreements described above and the restrictions of Rule 144 in the case of our affiliates.

Additionally, after this offering, the holders of an aggregate of 13,832,226 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.

***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 as they will be in effect following this offering 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 will have 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 will 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.***

Upon the closing of this offering, our executive officers, directors and current beneficial owners of 5% or more of our common stock and their respective affiliates beneficially own 61% 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. In addition, certain of our existing stockholders, including entities affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of approximately $25.0 million in shares of our common stock in this offering at the initial public offering price per share. These indications of interest are not binding agreements or commitments to purchase, and accordingly the underwriters may determine to sell more, less or no shares in this offering to any of these persons or entities, or any of these persons or entities may determine to purchase more, less or no shares in this offering.

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 price at which shares are being sold in this offering and have held their shares for a longer period, they may be more interested in selling our company to an acquirer than other investors, or they may want us to pursue strategies that deviate from the interests of other stockholders.

***We are an "emerging growth company" and, as a result of the reduced disclosure and governance requirements applicable to emerging growth 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:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure in this prospectus;

- 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 this 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.

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

After the closing of this offering, we will be 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. Prior to this offering, 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 other regulatory authorities.

***We will have broad discretion in the use of proceeds from this offering and may invest or spend the proceeds in ways with which you do not agree and in ways that may not increase the value of your investment.***

We will have broad discretion over the use of proceeds from this offering. You may not agree with our decisions, and our use of the proceeds may not yield any return on your investment. We expect to use the net proceeds to us from this offering, together with 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 the proceeds from this offering to pursue our strategy to in-license or acquire additional product candidates. Our failure to apply the net proceeds from this offering 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 net proceeds. You will not have the opportunity to influence our decisions on how to use our net proceeds from this offering.

***The recently passed comprehensive tax reform bill could adversely affect our business and financial condition.***

On December 22, 2017, President Trump signed into law new legislation that significantly revises the U.S. Internal Revenue Code of 1986, as amended. The newly enacted federal income tax law, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), 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. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain how various states will respond to the newly enacted federal tax law. 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.***

As of December 31, 2017, we had federal and state net operating loss carryforwards of $91.5 million and $86.4 million, respectively. The federal and state net operating loss carryforwards will begin to expire, if not utilized, by 2022 and 2029, respectively. These net operating loss carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the newly enacted federal income tax law, 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 newly enacted federal tax law. 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 in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. If an ownership change occurs and our ability to use our net operating loss carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations.

***Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, will be your sole source of gains and you may never receive a return on your investment.***

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

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

As a public company listed in the United States, we will incur 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 expenses 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.

## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements that involve substantial risks and uncertainties. The forward-looking statements are contained principally in the sections of this prospectus entitled "Prospectus Summary," "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business," but are also contained elsewhere in this prospectus. In some cases, you can identify forward-looking statements by the words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "objective," "ongoing," "plan," "predict," "project," "potential," "should," "will," or "would," or the negative of these terms, or other comparable terminology intended to identify statements about the future. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements. In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. Forward-looking statements include statements regarding:

- the timing, progress and results of our clinical trials of PB2452, PB1046 and any other product candidates, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available and our research and development programs;
- the timing of any submission of filings for regulatory approval of PB2452 and PB1046 and our ability to obtain and maintain regulatory approvals for PB2452 and PB1046 for any indication;
- our expectations regarding the size of the patient populations, market acceptance and opportunity for and clinical utility of our product candidates, if approved for commercial use;
- our manufacturing capabilities and strategy, including the scalability and commercial viability of our manufacturing methods and processes;
- our expectations regarding the scope of any approved indication for PB2452 and PB1046;
- our ability to successfully commercialize our product candidates;
- our ability to leverage our proprietary ELP technology to identify and develop future product candidates;
- our estimates of our expenses, ongoing losses, future revenue, capital requirements and our needs for or ability to obtain additional funding;
- our ability to establish or maintain collaborations or strategic relationships;
- our ability to identify, recruit and retain key personnel;
- our ability to protect and enforce our intellectual property position for our product candidates, and the scope of such protection;
- our financial performance;
- our expected use of proceeds from this offering;
- our competitive position and the development of and projections relating to our competitors or our industry;
- our estimates regarding future revenue, expenses and needs for additional financing; the impact of laws and regulations;

- the impact of laws and regulations;
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act; and
- the potential purchases by certain of our existing stockholders, including entities affiliated with certain of our directors, in this offering.

We caution you that the foregoing list may not contain all of the forward-looking statements made in this prospectus.

You should refer to the "Risk Factors" section of this prospectus for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. We have based the forward-looking statements contained in this prospectus primarily on our current expectations and projections about future events and trends that we believe may affect our business, financial condition, results of operations and prospects. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions, as a result we cannot assure you that the forward-looking statements in this prospectus will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law. The Private Securities Litigation Reform Act of 1995 and Section 27A of the Securities Act do not protect any forward-looking statements that we make in connection with this offering.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

## INDUSTRY AND MARKET DATA

We obtained the industry, statistical and market data in this prospectus from our own internal estimates and research as well as from industry and general publications and research, surveys and studies conducted by third parties. All of the market data used in this prospectus involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. While we believe that each of these studies and publications is reliable, the industry in which we operate is subject to a high degree of uncertainty and risk due to a variety of important factors, including those described in the section titled "Risk Factors." These and other factors could cause results to differ materially from those expressed in the estimates made by third parties and by us.

## USE OF PROCEEDS

We estimate that the net proceeds from our issuance and sale of 5,000,000 shares of our common stock in this offering will be approximately $57.9 million (or $67.0 million if the underwriters exercise in full their option to purchase additional shares to cover over-allotments), assuming an initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Each $1.00 increase (decrease) in the assumed initial public offering price of $13.00 per share would increase (decrease) the net proceeds to us from this offering by approximately $4.7 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each increase (decrease) of 1.0 million in the number of shares we are offering would increase (decrease) the net proceeds to us from this offering, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, by approximately $12.1 million, assuming the assumed initial public offering price stays the same.

As of June 30, 2018, we had $8.7 million in cash and cash equivalents. In August 2018, we received $17.7 million in net proceeds from the sale of our Series D redeemable convertible preferred stock and we received $2.0 million in additional borrowings under our loan and security agreement with Silicon Valley Bank. We intend to use the net proceeds from this offering, together with our existing cash, as follows:

- approximately $37.0 million to $39.0 million to advance PB2452;
- approximately $11.0 million to $13.0 million to advance PB1046;
- approximately $12.0 million to $14.0 million to fund development of our ELP technology and preclinical programs; and
- the remainder for working capital and other general corporate purposes.

We believe that the net proceeds of this offering, together with our existing cash, will enable us to fund our operations into the third quarter of 2020. Based on our current operational plans and assumptions, we expect our cash and cash equivalents, together with the net proceeds from this offering, will be sufficient to complete our Phase 2a and Phase 2 clinical trials for PB2452, initiate our Phase 3 clinical trial for PB2452, manufacture drug supply for Phase 2 and Phase 3 clinical trials and related commercial manufacturing activities for PB2452, including scale-up, process characterization and validation, complete our Phase 2b clinical trial for PB1046 and complete IND-enabling studies for one additional preclinical product candidate. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we expect.

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

Our management will have broad discretion in the application of the net proceeds from this offering, and investors will be relying on the judgment of our management regarding the application of those net proceeds. The timing and amount of our actual expenditures will be based on many factors, including cash flows from operations and the anticipated growth of our business. Pending these uses, we plan to invest these net proceeds in short-term, interest bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the United States.

## DIVIDEND POLICY

We have never declared or paid, and do not anticipate declaring or paying, in the foreseeable future, any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business. Any future determination related to our dividend policy will be made at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, contractual restrictions, business prospects and other factors our board of directors may deem relevant.

## CAPITALIZATION

The following table sets forth our cash and cash equivalents and our capitalization as of June 30, 2018:

- on an actual basis;
- on a pro forma basis to reflect: (1) the automatic conversion of all outstanding shares of our redeemable convertible preferred stock, including the conversion of 3,923,168 shares of Series D redeemable convertible preferred stock that we issued in August 2018, into an aggregate of 13,064,781 shares of common stock, based on an assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, as if such conversion had occurred on June 30, 2018; (2) the exercise of outstanding warrants to purchase 777,835 shares of our redeemable convertible preferred stock, including warrants to purchase 368,582 shares of Series C-1 redeemable convertible preferred stock that we issued in August 2018 in conjunction with the issuance of our Series D redeemable convertible preferred stock, and the automatic conversion thereof into 777,835 shares of common stock, which we expect will occur immediately prior to the closing of this offering; (3) the receipt of $17.7 million in net proceeds from our sale of Series D redeemable convertible preferred stock; (4) the conversion of our outstanding convertible promissory notes, and accrued interest thereon; and (5) the receipt of $2.0 million in additional borrowings under the loan and security agreement with Silicon Valley Bank; and
- on a pro forma as adjusted basis to give further effect to (1) our issuance and sale of shares of common stock in this offering at an assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us and (2) the filing of our amended and restated certificate of incorporation immediately prior to the closing of this offering.

You should read this table together with "Selected Financial Data," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and the related notes appearing at the end of this prospectus.

| | As of June 30, 2018 | | |
|---|---|---|---|
| | Actual | Pro Forma | Pro Forma As Adjusted |
| **(in thousands, except share and per share data)** | | | |
| Cash and cash equivalents | $ 8,734 | $ 28,446 | $ 86,352 |
| Convertible promissory notes, net of discount | 14,140 | — | — |
| Long-term debt, including current portion | 5,490 | 7,490 | 7,490 |
| Redeemable convertible preferred stock, $0.001 par value; 18,292,703 shares authorized, actual and pro forma; 9,131,999 shares issued and outstanding, actual; no shares issued and outstanding, pro forma; no shares authorized, issued or outstanding, pro forma as adjusted | 89,667 | — | — |
| Stockholders' (deficit) equity: | | | |
| Common stock, $0.001 par value; 20,789,273 shares authorized, actual and pro forma; 745,788 shares outstanding, actual; 14,588,404 shares outstanding, pro forma; 200,000,000 shares authorized, pro forma as adjusted; 19,588,404 shares outstanding, pro forma as adjusted | 1 | 15 | 20 |
| Treasury stock, at cost, 29,967 shares | (24) | (24) | (24) |
| Additional paid-in capital | 1,805 | 130,505 | 188,400 |
| Accumulated deficit | (110,142) | (110,142) | (110,142) |
| Total stockholders' (deficit) equity | $(108,360) | $ 20,354 | $ 78,254 |
| Total capitalization | $ 937 | $ 27,844 | $ 85,744 |

The pro forma as adjusted capitalization information discussed above is illustrative only and will change based on the actual initial public offering price. Each $1.00 increase (decrease) in the assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, additional paid-in capital, total stockholders' (deficit) equity and total capitalization by $4.7 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. A 1,000,000 share increase in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase the pro forma as adjusted amount of each of cash and cash equivalents, additional paid-in capital, total stockholders' equity (deficit) and total capitalization by $12.1 million, assuming the assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The outstanding share information in the table above excludes:

- 1,210,776 shares of common stock issuable upon the exercise of options outstanding as of June 30, 2018, at a weighted-average exercise price of $1.68 per share;
- 90,256 shares of common stock reserved for future issuance under our 2002 Plan as of June 30, 2018, which shares will cease to be available for issuance at the time our 2018 Plan becomes effective;
- 75,597 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2018, at a weighted-average exercise price of $9.659 per share, which warrants are expected to remain outstanding following the closing of this offering;
- 1,878,041 shares of common stock reserved for future issuance under our 2018 Plan; and
- 196,000 shares of common stock reserved for future issuance pursuant to our 2018 Employee Stock Purchase Plan, which will become effective prior to the closing of this offering.

## DILUTION

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

Our historical net tangible book value deficit as of June 30, 2018 was $(108.4) million, or $(145.29) per share of common stock. Our historical net tangible book value deficit per share represents our total tangible assets less our total liabilities and redeemable convertible preferred stock (which is not included within stockholders' deficit), divided by the number of shares of common stock outstanding as of June 30, 2018.

Our pro forma net tangible book value as of June 30, 2018 was $20.4 million, or $1.40 per share of common stock. Pro forma net tangible book value per share represents our total tangible assets less our total liabilities, divided by the number of shares of common stock outstanding as of June 30, 2018, after giving effect to (1) the automatic conversion of all outstanding shares of our redeemable convertible preferred stock, including the conversion of 3,923,168 shares of Series D redeemable convertible preferred stock that we issued in August 2018, into an aggregate of 13,064,781 shares of common stock, based on an assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, as if such conversion had occurred on June 30, 2018, (2) the exercise of outstanding warrants to purchase 777,835 shares of our redeemable convertible preferred stock, including warrants to purchase 368,582 shares of Series C-1 redeemable convertible preferred stock that we issued in August 2018 upon the conversion of our outstanding convertible promissory notes, and the automatic conversion thereof into 777,835 shares of common stock, which we expect to occur immediately prior to the closing of this offering, (3) the receipt of $17.7 million in net proceeds from our sale of Series D redeemable convertible preferred stock; (4) the conversion of our outstanding convertible promissory notes, and accrued interest thereon, as if such events had occurred on June 30, 2018; and (5) the receipt of $2.0 million in additional borrowings under the loan and security agreement with Silicon Valley Bank.

After giving further effect to the sale of 5,000,000 shares of common stock in this offering at an assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of June 30, 2018 was $78.3 million, or $3.99 per share of common stock. This amount represents an immediate increase in pro forma net tangible book value of $2.59 per share to our existing stockholders and an immediate dilution of $9.01 per share to investors participating in this offering. We determine dilution per share to investors participating in this offering by subtracting pro forma as adjusted net tangible book value per share after this offering from the assumed initial public offering price per share paid by investors participating in this offering.

The following table illustrates this dilution on a per share basis to new investors:

| | | |
|---|---|---|
| Assumed initial public offering price per share | | $13.00 |
| Historical net tangible book value (deficit) per share as of June 30, 2018 | $(145.29) | |
| Increase per share attributable to the pro forma transactions described above | 146.69 | |
| Pro forma net tangible book value per share as of June 30, 2018 | $ 1.40 | |
| Increase in pro forma net tangible book value per share attributable to the sale of shares in this offering | 2.59 | |
| Pro forma as adjusted net tangible book value per share after giving effect to this offering | | $ 3.99 |
| Dilution per share to new investors in this offering | | $ 9.01 |

The pro forma as adjusted dilution information discussed above is illustrative only and will change based on the actual initial public offering price. Each $1.00 increase (decrease) in the assumed initial public offering price

of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted net tangible book value per share by $0.24 per share and the dilution per share to investors participating in this offering by $0.76 per share, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. A 1,000,000 share increase in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase the pro forma as adjusted net tangible book value per share by $0.40 and decrease the dilution per share to new investors participating in this offering by $0.40, assuming the assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. A 1,000,000 share decrease in the number of shares offered by us, as set forth on the cover page of this prospectus, would decrease the pro forma as adjusted net tangible book value per share after this offering by $0.43 and increase the dilution per share to new investors participating in this offering by $0.43, assuming the assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

If the underwriters exercise their over-allotment option in full to purchase an additional 750,000 shares of our common stock in this offering, the pro forma as adjusted net tangible book value of our common stock would be $4.29 per share, the increase in pro forma net tangible book value per share would be $2.89 per share and the dilution per share to new investors would be $8.71 per share, in each case assuming an initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus.

The following table summarizes as of June 30, 2018, on the pro forma as adjusted basis described above, the number of shares of our common stock, the total consideration and the average price per share (1) paid to us by our existing stockholders and (2) to be paid by investors purchasing our common stock in this offering at an assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, before deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

| | Shares Purchased | | Total Consideration | | Average Price Per Share |
|---|---|---|---|---|---|
| | Number | Percent | Amount | Percent | |
| Existing stockholders | 14,588,404 | 74.5% | $123,040,646 | 65.4% | $ 0.12 |
| New investors | 5,000,000 | 25.5 | 65,000,000 | 34.6 | 13.00 |
| Total | 19,588,404 | 100.0% | $188,040,646 | 100.0% | |

The outstanding share information used in the computations above excludes:

- 1,210,776 shares of common stock issuable upon the exercise of options outstanding as of June 30, 2018, at a weighted-average exercise price of $1.68 per share;
- 90,256 shares of common stock reserved for future issuance under our 2002 Plan as of June 30, 2018, which shares will cease to be available for issuance at the time our 2018 Plan becomes effective;
- 75,597 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2018, at a weighted-average exercise price of $9.659 per share, which warrants are expected to remain outstanding following the closing of this offering;
- 1,878,041 shares of common stock reserved for future issuance under our 2018 Plan; and

- 196,000 shares of common stock reserved for future issuance pursuant to our 2018 Employee Stock Purchase Plan, which will become effective prior to the closing of this offering.

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

Certain of our existing stockholders, including entities affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of approximately $25.0 million in shares of our common stock in this offering at the initial public offering price per share. Based on an assumed initial public offering price of $13.00 per share, these persons and entities would purchase an aggregate of approximately 1,900,000 of the 5,000,000 shares in this offering based on these indications of interest. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any of these persons or entities, or any of these persons or entities may determine to purchase more, less or no shares in this offering. The foregoing discussion and tables do not reflect any potential purchases by these persons or entities or their affiliated entities.

## SELECTED FINANCIAL DATA

You should read the following selected financial data together with our financial statements and the related notes thereto appearing at the end of this prospectus and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus. We have derived the statements of operations data for the years ended December 31, 2016 and 2017 and the balance sheet data as of December 31, 2016 and 2017 from our audited financial statements appearing at the end of this prospectus. The statements of operations data for the six months ended June 30, 2017 and 2018 and the balance sheet data as of June 30, 2018 have been derived from our unaudited interim financial statements appearing at the end of this prospectus and have been prepared on the same basis as the audited financial statements. In the opinion of management, the unaudited data reflects all adjustments, consisting only of normal recurring adjustments, considered necessary for a fair presentation of the financial information in those statements. Our historical results are not necessarily indicative of the results that should be expected in the future and the results for the six months ended June 30, 2018 are not necessarily indicative of the results to be expected for the full year ending December 31, 2018 or any other future period.

| | Year Ended December 31, | | Six Months Ended June 30, | |
|---|---|---|---|---|
| | 2016 | 2017 | 2017 | 2018 |
| | (in thousands, except share and per share data) | | (unaudited) | |
| **Statements of Operations Data:** | | | | |
| Operating expenses: | | | | |
| Research and development | $ 7,376 | $ 6,210 | $ 3,057 | $ 5,425 |
| General and administrative | 2,125 | 2,328 | 1,135 | 1,560 |
| Total operating expenses | 9,501 | 8,538 | 4,192 | 6,985 |
| Loss from operations | (9,501) | (8,538) | (4,192) | (6,985) |
| Other income (expense): | | | | |
| Interest income | 29 | 52 | 15 | 72 |
| Interest expense | — | (2,723) | (987) | (2,851) |
| Change in fair value of warrant liability | 252 | 1,019 | 125 | (996) |
| Change in fair value of derivative liability | — | (57) | (113) | (317) |
| Total other income (expense) | 281 | (1,709) | (960) | (4,092) |
| Net loss | $ (9,220) | $ (10,247) | $ (5,152) | $ (11,077) |
| Net loss per common share, basic and diluted[1] | $ (12.41) | $ (13.78) | $ (6.93) | $ (14.85) |
| Weighted-average common shares outstanding, basic and diluted[1] | 742,808 | 743,470 | 743,241 | 745,788 |
| Pro forma net loss per common share, basic and diluted (unaudited)[1] | | $ (0.76) | | $ (0.58) |
| Pro forma weighted-average common shares outstanding, basic and diluted (unaudited)[1] | | 11,235,815 | | 12,376,871 |

(1) See Note 2 to our financial statements appearing at the end of this prospectus for an explanation of the method used to calculate the historical and pro forma net loss per common share, basic and diluted.

| | As of December 31, | | As of June 30, |
|---|---|---|---|
| | 2016 | 2017 | 2018 |
| | | (in thousands) | (unaudited) |
| **Balance Sheet Data:** | | | |
| Cash and cash equivalents | $ 3,715 | $ 13,406 | $ 8,734 |
| Working capital (deficit)[1] | 3,040 | (3,849) | (14,348) |
| Total assets | 4,117 | 14,099 | 9,889 |
| Convertible promissory notes | — | 12,095 | 14,140 |
| Long-term debt, including current portion | — | 3,386 | 5,490 |
| Redeemable convertible preferred stock | 89,567 | 89,634 | 89,667 |
| Total stockholders' equity (deficit) | (87,182) | (97,416) | (108,360) |

(1) We define working capital (deficit) as total current assets less total current liabilities. See our financial statements appearing at the end of this prospectus for further details regarding our current assets and current liabilities.

## 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 the section titled "Selected Financial Data" and our financial statements and related notes included elsewhere in this prospectus. This discussion contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those discussed below. Factors that could cause or contribute to such difference include, but are not limited to, those identified below and those discussed in the section titled "Risk Factors" included elsewhere in this prospectus.*

### Overview

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

We have a limited operating history. Since our inception in 2002, our operations have focused on developing our clinical and preclinical product candidates and our proprietary ELP technology, organizing and staffing our company, business planning, raising capital, establishing our intellectual property portfolio and conducting clinical trials and preclinical studies. We do not have any product candidates approved for sale and have not generated any revenue from product sales. We have funded our operations primarily through the sale of equity. Since our inception, we have raised an aggregate of $121.7 million of gross proceeds from the sale of convertible debt, shares of our preferred stock and warrants to purchase shares of our redeemable convertible preferred stock.

Since our inception, we have incurred significant operating losses. Our net losses were $9.2 million and $10.2 million for the years ended December 31, 2016 and 2017, respectively, and $11.1 million for the six months ended June 30, 2018. As of June 30, 2018, we had an accumulated deficit of $110.1 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 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.

**Financial Overview**

***Research and Development Expenses***

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

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

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect our research and development expenses 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 clinical trials and prepare regulatory filings for our product candidates.

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

- delays in regulators or institutional review boards authorizing us or our investigators to commence our clinical trials or in our ability to negotiate agreements with clinical trial sites or contract research organizations;
- our ability to secure adequate supply of 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 Expenses***

General and administrative expenses consist 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 expenses include professional fees for legal, accounting and tax-related services and insurance costs.

We anticipate that our general and administrative expenses 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 expenses 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 with Silicon Valley Bank.

***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.

**License Agreements**

***MedImmune Limited***

In November 2017, we entered into an exclusive license agreement with MedImmune Limited, a wholly owned subsidiary of AstraZeneca plc, or the MedImmune License. Pursuant to the MedImmune License, MedImmune granted us an exclusive, worldwide license under certain patent rights owned or controlled by MedImmune to develop and commercialize any products covered by the MedImmune License, or the MedImmune licensed products, for the treatment, palliation, diagnosis or prevention of any human disorder or condition. 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 June 30, 2018, we have paid $0.6 million under the MedImmune License, including $0.5 million in third party storage costs.

***Duke University***

In October 2006, we entered into an exclusive license agreement with Duke University, or the Duke License, which we most recently amended in May 2017. Pursuant to the Duke License, Duke granted us an exclusive, worldwide license under certain patent rights owned or controlled by Duke, and a non-exclusive, worldwide license under certain know-how of Duke, to develop and commercialize any products covered by the Duke License, or Duke licensed products, relating to ELPs. Under the Duke License, we paid Duke an upfront fee of $37,000, additional fees in connection with amendments to the Duke License of $0.2 million and other additional licensing fees of $0.2 million. In consideration for license rights granted to us, we initially issued Duke 24,493 shares of our common stock. Until we reached a certain stipulated equity milestone, which we reached in October 2007, we were obligated to issue additional shares of common stock to Duke from time to time so that its aggregate ownership represented 7.5% of our issued and outstanding capital stock. We are also required to pay Duke: up to $2.2 million in regulatory and clinical milestone fees; up to $0.4 million in commercial milestone fees; low single-digit royalty percentages on net sales of Duke licensed products, with minimum aggregate royalty payments of $0.2 million payable following our achievement of certain commercial milestones; and up to the greater of $0.3 million or a low double-digit percentage of the fees we receive from a third party in consideration of forming a strategic alliance with respect to certain patent rights covered under the Duke License. We also must pay Duke the first $1.0 million of non-royalty payments we receive from a sublicensee, and thereafter a low double-digit percentage of any additional nonroyalty payments we receive. As of June 30, 2018, we have not paid any amounts under the Duke License. We are required to apply for, prosecute and maintain all U.S. and foreign patent rights under the Duke License. As of June 30, 2018, we have incurred $1.0 million in patent prosecution costs under the Duke License.

**Results of Operations**

***Comparison of the Six Months Ended June 30, 2017 and 2018***

The following table summarizes our results of operations for the six months ended June 30, 2017 and 2018 (in thousands):

| | Six Months Ended June 30, | | |
|---|---|---|---|
| | **2017** | **2018** | **Change** |
| | **(unaudited)** | | |
| Operating expenses | | | |
| Research and development | $ 3,057 | $ 5,425 | $ 2,368 |
| General and administrative | 1,135 | 1,560 | 425 |
| Total operating expenses | 4,192 | 6,985 | 2,793 |
| Loss from operations | (4,192) | (6,985) | (2,793) |
| Other income (expense) | | | |
| Interest income | 15 | 72 | 57 |
| Interest expense | (987) | (2,851) | (1,864) |
| Change in fair value of warrant liability | 125 | (996) | (1,121) |
| Change in fair value of derivative liability | (113) | (317) | (204) |
| Total other expense, net | (960) | (4,092) | (3,132) |
| Net loss | $ (5,152) | $ (11,077) | $ (5,925) |

***Research and Development Expense***

Research and development expense was $3.1 million for the six months ended June 30, 2017, compared to $5.4 million for the six months ended June 30, 2018. The increase of $2.4 million was primarily attributable to

increased costs associated with clinical development activities as a result of increased clinical trial activities relating to PB1046 and PB2452.

The following table summarizes our research and development expenses by functional area for the six months ended June 30, 2017 and 2018 (in thousands):

| | Six Months Ended June 30, | |
|---|---|---|
| | 2017 | 2018 |
| Preclinical and clinical development | $ 1,412 | $ 3,706 |
| Compensation and related benefits | 1,278 | 1,277 |
| Stock-based compensation | 18 | 112 |
| Facilities expense | 190 | 202 |
| Other | 159 | 128 |
| Total research and development expenses | $ 3,057 | $ 5,425 |

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 six months ended June 30, 2017 and 2018 (in thousands):

| | Six Months Ended June 30, | |
|---|---|---|
| | 2017 | 2018 |
| External research and development expense by program | | |
| PB1046 | $ 1,078 | $ 1,278 |
| PB2452 | — | 1,572 |
| Unallocated research and development expense | | |
| Other research and development | 683 | 1,186 |
| Compensation and stock-based compensation | 1,296 | 1,389 |
| Total research and development expenses | $ 3,057 | $ 5,425 |

***General and Administrative Expense***

General and administrative expense was $1.1 million for the six months ended June 30, 2017, compared to $1.6 million for the six months ended June 30, 2018. The increase of $0.4 million was primarily attributable to increases in patent costs, related legal fees and other outside professional services.

***Interest Expense***

Interest expense was $1.0 million for the six months ended June 30, 2017, compared to $2.9 million for the six months ended June 30, 2018. The increase of $1.9 million was attributable to an additional $8.1 million in borrowings pursuant to our convertible promissory notes and our term loan with Silicon Valley Bank, which we entered into in October 2017.

***Change in Fair Value of Warrant Liability***

Change in fair value of warrant liability resulted in other income of $0.1 million for the six months ended June 30, 2017, compared to other expense of $1.0 million for the six months ended June 30, 2018. The preferred

stock warrants are subject to remeasurement at each reporting period, with changes in fair value recorded in the statement of operations.

***Change in Fair Value of Derivative Liability***

Change in fair value of derivative liability resulted in other expense of $0.1 million for the six months ended June 30, 2017, compared to other expense of $0.3 million for the six months ended June 30, 2018. The conversion option related to our convertible promissory notes is subject to remeasurement at each reporting period, with changes in fair value recorded in the statement of operations.

***Comparison of the Years Ended December 31, 2016 and 2017***

The following table summarizes our results of operations for the years ended December 31, 2016 and 2017 (in thousands):

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2016 | 2017 | Change |
| Operating expenses | | | |
| Research and development | $ 7,376 | $ 6,210 | $ (1,166) |
| General and administrative | 2,125 | 2,328 | 203 |
| Total operating expenses | 9,501 | 8,538 | (963) |
| Loss from operations | (9,501) | (8,538) | 963 |
| Other income (expense) | | | |
| Interest income | 29 | 52 | 23 |
| Interest expense | — | (2,723) | (2,723) |
| Change in fair value of warrant liability | 252 | 1,019 | 767 |
| Change in fair value of derivative liability | — | (57) | (57) |
| Total other income (expense), net | 281 | (1,709) | (1,990) |
| Net loss | $ (9,220) | $ (10,247) | $ (1,027) |

***Research and Development Expense***

Research and development expense was $7.4 million for the year ended December 31, 2016, compared to $6.2 million for the year ended December 31, 2017. The decrease of $1.2 million was primarily attributable to a decrease in preclinical and clinical development activities due to the discontinuation of a prior clinical program at the end of 2016.

The following table summarizes our research and development expenses by functional area for the years ended December 31, 2016 and 2017 (in thousands):

| | Year Ended December 31, | |
|---|---|---|
| | 2016 | 2017 |
| Preclinical and clinical development | $ 4,372 | $ 2,944 |
| Compensation and related benefits | 2,309 | 2,473 |
| Stock-based compensation | 101 | 37 |
| Facilities expense | 383 | 389 |
| Other | 211 | 367 |
| Total research and development expenses | $ 7,376 | $ 6,210 |

The following table summarizes our research and development expenses by product candidate for the years ended December 31, 2016 and 2017 (in thousands):

| | Year Ended December 31, | |
|---|---|---|
| | 2016 | 2017 |
| External research and development expense by program | | |
| PB1046 | $ 2,068 | $ 1,918 |
| PB2452 | — | 579 |
| Unallocated research and development expense | | |
| Other research and development | 2,898 | 1,203 |
| Compensation and stock-based compensation | 2,410 | 2,510 |
| Total research and development expenses | $ 7,376 | $ 6,210 |

***General and Administrative Expense***

General and administrative expense was $2.1 million for the year ended December 31, 2016, compared to $2.3 million for the year ended December 31, 2017. The increase of $0.2 million was primarily attributable to an increase in compensation expense of $0.2 million and legal costs of $0.2 million, partially offset by a decrease in other outside services and business expenses of $0.2 million.

***Interest Expense***

There was no interest expense for the year ended December 31, 2016, compared to $2.7 million of interest expense for the year ended December 31, 2017, which was due to borrowing on convertible promissory notes and our term loan, all entered into during the year ended December 31, 2017.

***Change in Fair Value of Warrant Liability***

The change in fair value of warrant liability was $0.3 million for the year ended December 31, 2016, compared to a $1.0 million for the year ended December 31, 2017. The preferred stock warrants are subject to remeasurement at each reporting period, with changes in fair value recorded in the statement of operations.

***Change in Fair Value of Derivative Liability***

There was no change in fair value of derivative liability for the year ended December 31, 2016, compared to a $0.1 million for the year ended December 31, 2017. The conversion option on our convertible promissory notes is subject to remeasurement at each reporting period, with changes in fair value recorded in the statement of operations.

**Liquidity and Capital Resources**

Since our inception, we have not generated any revenue and have incurred net losses and negative cash flows from our operations. We have financed our operations since our inception through sales of our convertible debt, convertible preferred stock and warrants to purchase shares of our redeemable convertible preferred stock, receiving aggregate gross proceeds of $121.7 million.

In October 2017, we entered into a loan and security agreement, or the SVB Loan, with Silicon Valley Bank, or SVB, which provides that we may borrow up to $7.5 million, issuable in three separate tranches, or Growth Capital Advances, of $3.5 million, $2.0 million and $2.0 million, each available upon achievement of certain clinical and regulatory milestones. We drew the first $3.5 million tranche in November 2017.

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

SVB Loan, we made interest-only payments through June 30, 2018 at a rate equal to the Prime Rate, as defined in the SVB Loan. The SVB Loan is interest-only through July 31, 2018, which will be extended to December 31, 2018 if we borrow 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 addition to interest and principal payments, we are required to make a final payment equal to 7% of the original aggregate principal amount of the Growth Capital Advances. We have the option to prepay all, but not less than all, of the borrowed amounts, provided that we would be obligated to pay a prepayment fee equal to (a) 3.0% of the outstanding principal balance of the applicable Growth Capital Advances if prepayment is 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 is 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 is made after the second anniversary of the effective date of the SVB Loan.

In April 2018, the SVB Loan was amended to: (a) extend the draw period of the final two tranches to April 30, 2018 and July 31, 2018, respectively and (b) extend the interest only period. Following the amendment, we drew the $2.0 million tranche in April 2018. Pursuant to the SVB Loan, the maturity date is June 1, 2020 unless we borrow the third tranche, which would result in an extension of the maturity date to December 31, 2020.

In July 2018, the SVB Loan was again amended to extend the draw period of the final tranche to August 31, 2018, as well as extend the interest-only period of the SVB Loan through August 31, 2018, which will be extended to December 31, 2018 if we draw the final tranche. In August 2018, we borrowed $2.0 million under the final tranche.

In January 2017 and October 2017, we issued $14.7 million of convertible promissory notes, or the 2017 Notes, to holders of Series C-1 redeemable convertible preferred stock. The 2017 Notes bore interest at the rate of 8%. Upon a subsequent equity financing of at least $10.0 million prior to the stated maturity date of March 31 2018, the 2017 Notes plus accrued interest would automatically convert into shares of the stock issued by us in such financing at a price equal to 80% of the lowest issue price. In the event that the equity financing was less than $10.0 million, or did not occur prior to the stated maturity date, the 2017 Notes, upon written consent of our board of directors, our largest stockholder and holders of a majority of the principal amount of the then outstanding 2017 Notes, could either (a) convert the principal plus accrued interest on the 2017 Notes into shares of the stock issued in such financing at a price equal to 80% of the lowest issue price, (b) convert the principal amount plus accrued interest into shares of Series C-1 redeemable convertible preferred stock at $9.659 per share or (c) the 2017 Notes become immediately due and payable.

The 2017 Notes had a stated maturity date of March 31, 2018. In October 2017, the noteholders entered into a subordination agreement with SVB. Under the terms of the subordination agreement, the noteholders would not demand or receive any payment on the 2017 Notes until all amounts owed under the SVB Loan were repaid in full on June 1, 2020.

As of June 30, 2018, we had cash and cash equivalents of $8.7 million. 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 2,080,209 shares of Series D redeemable convertible preferred stock.

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

| | Year Ended December 31, | | Six Months Ended June 30, | |
|---|---|---|---|---|
| | 2016 | 2017 | 2017 | 2018 |
| | | | (unaudited) | |
| Net cash used in operating activities | $ (9,688) | $ (8,259) | $ (3,745) | $ (6,639) |
| Net cash provided by (used in) investing activities | 9,249 | (216) | (67) | (28) |
| Net cash provided by financing activities | 1 | 18,166 | 6,601 | 1,995 |
| Net increase (decrease) in cash and cash equivalents | $ (438) | $ 9,691 | $ 2,789 | $ (4,672) |

***Operating Activities***

Net cash used in operating activities was $3.7 million during the six months ended June 30, 2017, as compared to $6.6 million during the six months ended June 30, 2018. Net cash used in operating activities was $9.7 million during the year ended December 31, 2016 as compared to $8.3 million during the year ended December 31, 2017. The primary use of cash was to fund our operations related to the development of our product candidates in each of these periods.

***Investing Activities***

Net cash used in investing activities was $67,000 during the six months ended June 30, 2017, as compared to $28,000 during the six months ended June 30, 2018, in both cases for the purchase of property and equipment. During the year ended December 31, 2016, investing activities provided cash of $9.2 million, primarily from net proceeds from the sale of short-term investments. During the year ended December 31, 2017, net cash used in investing activities was $0.2 million for the purchase of property and equipment.

***Financing Activities***

Net cash provided by financing activities was $6.6 million during the six months ended June 30, 2017, due to the issuance of convertible promissory notes. Net cash provided by financing activities was $2.0 million during the six months ended June 30, 2018 due to the issuance of the SVB Loan. During the year ended December 31, 2017, cash provided by financing activities was $18.2 million, consisting of the net proceeds from the issuance of convertible debt and the SVB Loan.

***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 few 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. Furthermore, following the completion of this offering, we expect to incur additional costs associated with operating as a public company. 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, together with the net proceeds from this offering, will enable us to fund our operating expenses and capital expenditure requirements into the third quarter of 2020. We intend to devote the majority of the net proceeds from this offering to the clinical and preclinical development of our product candidates. 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 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.

**Contractual Obligations, Commitments and Contingencies**

The following table summarizes our contractual obligations and commitments as of December 31, 2017 (in thousands):

| | Payments Due by Period | | | | |
|---|---|---|---|---|---|
| | Total | Less than 1 Year | 1-3 Years | 3-5 Years | More than 5 Years |
| Long-term debt, including interest and final payment obligations | $ 3,965 | $ 1,005 | $ 2,960 | $ — | $ — |
| Convertible promissory notes, including interest | 15,997 | 15,997 | — | — | — |
| Operating lease obligations | 1,501 | 262 | 507 | 529 | 203 |
| Total | $ 21,463 | $ 17,264 | $ 3,467 | $ 529 | $ 203 |

Our commitments for operating leases relate primarily to our lease of office space in Malvern, Pennsylvania.

Our commitment for long-term debt relates to the SVB Loan. As of June 30, 2018, we had borrowed $5.5 million under the SVB Loan. In August 2018, we borrowed an additional $2.0 million under the SVB Loan.

The contractual obligations table does not include any potential contingent payments upon the achievement by us of clinical, regulatory and commercial events, as applicable, or royalty payments that we may be required to make under license agreements we have entered into with various entities pursuant to which we have in-licensed certain intellectual property, including our license agreements with MedImmune and Duke University. We excluded the contingent payments given that the timing and amount (if any) of any such payments cannot be reasonably estimated at this time. See "Business—License Agreements" for additional information.

**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 Judgements and Estimates**

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to accrued expenses and stock-based compensation. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our financial statements appearing at the end of this prospectus, we believe the following accounting policies are the most critical to the judgments and estimates used in the preparation of our financial statements.

***Accrued Research and Development Expense***

The majority of our operating expenses to date have been incurred in research and development activities. As part of the process of preparing our financial statements, we are required to estimate expenses resulting from obligations under contracts with vendors, consultants and research organizations, in connection with conducting

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

***Stock-Based Compensation***

We measure and recognize compensation expense for all employee options based on the estimated fair value of the award on the grant date and non-employee options based on the estimated fair value of the award on the date when the options vest. We use the Black-Scholes option-pricing model to estimate the fair value of option awards. The fair value is recognized as expense on a straight-line basis over the requisite service period.

The Black-Scholes option-pricing model requires the use of subjective assumptions that include the expected stock price volatility and the fair value of the underlying common stock on the date of grant. See Note 10 to our financial statements appearing at the end of this prospectus for information concerning certain of the specific assumptions we used in applying the Black-Scholes option pricing model to determine the estimated fair value of our stock options granted during the periods ended December 31, 2016 and 2017 and for the six months ended June 30, 2017 and 2018.

The following table summarizes by grant date the number of shares of common stock underlying stock options granted from January 1, 2017 through the date of this prospectus and the associated per share exercise price and the estimated fair value per share of our common stock on the grant date:

| Grant Date | Number of Common Shares Underlying Options Granted | Exercise Price Per Share | Estimated Common Stock Fair Value Per Share at Date of Grant |
|---|---|---|---|
| April 21, 2017 | 85,859 | $ 1.44 | $ 1.44 |
| December 16, 2017 | 14,007 | $ 1.44 | $ 1.44 |
| May 3, 2018 | 135,567 | $ 2.22 | $ 2.22 |
| August 8, 2018 | 124,734 | $ 4.65 | $ 4.65 |

Total stock-based compensation expense included in the statement of operations was allocated as follows (in thousands):

| | Year Ended December 31, | | Six Months Ended June 30, | |
|---|---|---|---|---|
| | 2016 | 2017 | 2017 | 2018 |
| | | | (unaudited) | |
| General and administrative | $ 59 | $ 40 | $ 20 | $ 54 |
| Research and development | 101 | 37 | 18 | 112 |
| Total stock-based compensation | $ 160 | $ 77 | $ 38 | $ 166 |

Based on the assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, the intrinsic value of stock options outstanding as of June 30, 2018 was $13.7 million, of which $8.7 million and $5.0 million was related to stock options that were vested and unvested, respectively, at that date.

***Determination of the Fair Value of Common Stock***

We are required to estimate the fair value of the common stock underlying our stock-based awards when performing the fair value calculations using the Black-Scholes option pricing model. Because our common stock is not currently publicly traded, the fair value of the common stock underlying our stock-based awards has been determined on each grant date by our board of directors, with input from management, considering our most recently available third-party valuation of common shares. All options to purchase shares of our common stock are intended to be granted with an exercise price per share no less than the fair value per share of our common stock underlying those options on the date of grant, based on the information known to us on the date of grant.

The third-party valuation of our common stock was performed using methodologies, approaches and assumptions consistent with the American Institute of Certified Public Accountants, or AICPA, Audit and Accounting Practice Aid Series: Valuation of Privately Held Company Equity Securities Issued as Compensation, or the AICPA Practice Guide. In addition, our board of directors considered various objective and subjective factors to determine the fair value of our common stock, including:

- the estimated value of each security both outstanding and anticipated;
- the anticipated capital structure that will directly impact the value of the currently outstanding securities;
- our results of operations and financial position;
- the status of our research and development efforts;
- the composition of, and changes to, our management team and board of directors;
- the lack of liquidity of our common stock as a private company;
- our stage of development and business strategy and the material risks related to our business and industry;
- external market conditions affecting the life sciences and biotechnology industry sectors;
- U.S. and global economic conditions;
- the likelihood of achieving a liquidity event for the holders of our common stock, such as an initial public offering, or IPO, or a sale of our company, given prevailing market conditions; and
- the market value and volatility of comparable companies.

Following the closing of this offering, the fair value of our common stock will be the closing price of our common stock on the Nasdaq Global Market as reported on the date of the grant.

***Methods Used to Allocate Our Enterprise Value to Classes of Securities***

In accordance with the AICPA Practice Guide, we considered the various methods for allocating the enterprise value across our classes and series of capital stock to determine the fair value of our common stock at the valuation date. Under the option pricing method, shares are valued by creating a series of call options with exercise prices based on the liquidation preferences and conversion terms of each equity class. The values of the preferred and common stock are inferred by analyzing these options. The probability-weighted expected return method is a scenario-based analysis that estimates the value per share based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to us, as well as the economic and control rights of each share class.

There are significant judgments and estimates inherent in the determination of the fair value of our common stock. These judgments and estimates include assumptions regarding our future operating performance, the time to completing an IPO or other liquidity event and the determination of the appropriate valuation methods. If we had made different assumptions, our stock-based compensation expense, net loss and net loss per common share could have been significantly different.

## Other Information

### *Net Operating Loss and Research and Development Tax Credit Carryforwards*

As of December 31, 2017, we had federal and Pennsylvania tax net operating loss carryforwards of $91.5 million and $86.4 million, respectively, which begin to expire in 2022 and 2029, respectively, unless previously utilized. As of December 31, 2017, we also had federal and Pennsylvania research and development tax credit carryforwards of $3.1 million and $0.1 million, respectively. The federal research and development tax credit carryforwards will begin to expire in 2028 and 2029, respectively, unless previously utilized.

Utilization of the net operating losses and credits may be subject to a substantial annual limitation due to ownership change limitations provided by the Internal Revenue Code of 1986, as amended. The annual limitation may result in the expiration of our net operating losses and credits before we can use them. We have recorded a valuation allowance on all of our deferred tax assets, including our deferred tax assets related to our net operating loss and research and development tax credit carryforwards.

### *Recent Accounting Pronouncements*

See Note 2 to our financial statements appearing at the end of this prospectus for information concerning recent accounting pronouncements.

## Qualitative and Quantitative Disclosures about Market Risk

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.

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 years ended December 31, 2016 and 2017 or six months ended June 30, 2018.

## JOBS Act Transition Period

In April 2012, the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, was enacted. Section 107 of the JOBS Act provides that an "emerging growth company" can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended, for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

We are in the process of evaluating the benefits of relying on other exemptions and reduced reporting requirements under the JOBS Act. Subject to certain conditions, as an emerging growth company, we may rely on certain of these exemptions, including without limitation, (1) providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and (2) complying 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, known as the auditor discussion and analysis. We will remain an emerging growth company until the earlier to occur of (a) the last day of the fiscal year (i) following the fifth anniversary of the completion of this offering, (ii) in which we have total annual gross revenues of at least $1.07 billion or (iii) in which we are deemed to be a "large accelerated filer" under the rules of the U.S. Securities and Exchange Commission, 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 (b) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

# BUSINESS

## Overview

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

PB2452 is a novel recombinant human monoclonal antibody antigen-binding fragment, or Fab fragment, designed to reverse the antiplatelet activity of ticagrelor. Ticagrelor is an antiplatelet therapy widely prescribed to reduce the rates of death, heart attack and stroke in patients with acute coronary syndrome, or ACS, or who have previously experienced a heart attack. The American College of Cardiology, American Heart Association and European Society of Cardiology guidelines recognize ticagrelor as the preferred antiplatelet therapy for ACS. In 2017, ticagrelor, currently marketed by AstraZeneca plc, or AstraZeneca, under the brand names Brilinta and Brilique, had worldwide sales of over $1 billion, an increase of 29% over 2016 sales. In the first half of 2018, ticagrelor had worldwide sales of $609 million, an increase of 23% over sales in the first half of 2017. Ticagrelor binds to platelets to prevent them from forming blood clots, which could restrict blood flow to critical organs in these patients, causing heart attacks or strokes. Due to ticagrelor's antiplatelet activity, patients on ticagrelor have an elevated risk of spontaneous bleeding. In addition, patients on ticagrelor who need urgent surgery cannot wait the recommended five days for ticagrelor's effect to dissipate and are at increased risk of major bleeding during and after surgery. There are currently no known reversal agents approved or in clinical development for ticagrelor or any of the other antiplatelet drugs. In our Phase 1 clinical trial, PB2452 achieved rapid and complete reversal of ticagrelor's antiplatelet activity, with potential customizable duration of reversal based on the dosing regimen, which we believe has the potential to bring life-saving therapeutic benefit to these patients by increasing the safety of ticagrelor. We believe the availability of a reversal agent could expand ticagrelor's use by mitigating concerns regarding bleeding risk and uniquely position ticagrelor as the only oral antiplatelet drug with a reversal agent.

We recently completed a Phase 1 dose escalation clinical trial of PB2452 in healthy subjects ages 18 to 50 who had been pre-dosed with ticagrelor. In this trial, we observed rapid and complete reversal of ticagrelor's antiplatelet activity within five minutes following initiation of infusion, and sustained reversal for over 20 hours, in later dosing cohorts in which we administered PB2452 over an extended infusion period. Based on our observations in our Phase 1 trial, duration of reversal may be controlled by duration of the infusion, which may allow for customization based on patient needs. There were no PB2452-related adverse events, or AEs, or serious adverse events, or SAEs, in any of the completed dose cohorts. We believe that the results of the Phase 1 trial support the continued development of PB2452 to treat ticagrelor patients who are experiencing a major bleeding event or those who require urgent surgery.

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

Upon completion of the Phase 2a clinical trial, we intend to request a meeting with the U.S. Food and Drug Administration, or the FDA, to review the clinical profile of and confirm the regulatory pathway for PB2452.

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

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

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

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

We have an experienced management team that includes individuals with experience in translational research, orphan and cardiopulmonary drug discovery, development and commercialization. We are led by our Chief Executive Officer, Jonathan P. Mow, who brings more than 25 years of experience in biotechnology management, including previous executive experience at Amylin Pharmaceuticals, Corus Pharma, PathoGenesis and Bristol-Myers Squibb. We have been supported by a leading group of biotechnology investors, including funds and accounts managed by New Enterprise Associates, Hatteras Venture Partners, Johnson & Johnson Innovation — JJDC, Inc., Fletcher Spaght Ventures, Syno Capital, Astellas Venture Management, Cormorant

Asset Management, Rock Springs Capital and Mountain Group Partners, as well as AstraZeneca, from whom we licensed PB2452.

**Strategy**

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

- ***Continue to advance PB2452 through clinical development and regulatory approval***. We intend to develop and commercialize PB2452 as a novel reversal agent for the antiplatelet drug ticagrelor. We are conducting a Phase 1 dose escalation clinical trial of PB2452, delivered as an intravenous infusion, in healthy subjects that is designed to identify the dose and dosing regimen, determine proof of concept and evaluate the safety and tolerability of PB2452. Subject to discussions with the FDA, we intend to initiate a multi-center Phase 2 clinical trial in healthy older adults in the second half of 2019. Based on a planned interim assessment of an initial subset of patients in this trial, we plan to initiate an international, multi-center Phase 3 clinical trial in patients on ticagrelor who are experiencing a major bleeding event or require urgent surgery. If considered appropriate by the FDA, we intend to pursue accelerated approval, which would allow us to submit a BLA prior to completion of the Phase 3 clinical trial based on biomarker data from an initial subset of the Phase 3 patients.

- ***Continue to develop PB1046***. We intend to advance PB1046 through clinical trials as a once-weekly novel treatment for PAH that is vasodilatory, potentially disease-modifying and complementary to the current standard of care therapies. We are currently conducting a Phase 2b clinical trial of PB1046 and expect to report results from this trial in the first half of 2020. Based on the results of this trial, we intend to advance this product candidate into Phase 3 clinical development for the treatment of PAH.

- ***Broaden the potential therapeutic applications of PB1046***. Due to improvements in pharmacokinetics that we have observed with our ELP technology, we believe that the therapeutic potential of VIP can be applied to a variety of other orphan indications. Preclinical data suggest PB1046 may have clinical benefit in cardiomyopathy associated with Duchenne Muscular Dystrophy, or DMD, heart failure and other cardiomyopathies and in cystic fibrosis. As such, we intend to strategically broaden the therapeutic applications of PB1046 by exploring its development in additional indications.

- ***Leverage our ELP technology platform to expand our development pipeline***. We believe that our ELP technology enhances solubility, stability and bioavailability, provides extended drug exposure and creates product candidates that are straightforward to manufacture and administer. As such, we plan to utilize our platform to identify product candidates for additional orphan indications. We intend to apply our ELP technology to improve the pharmacokinetics of proteins and peptides with well-characterized therapeutic activities but suboptimal half-lives, in order to improve their pharmacokinetics, enable their use as pharmaceutical products and allow for more convenient dosing regimens.

- ***Commercialize our product candidates***. We have entered into exclusive license agreements with AstraZeneca for PB2452 and Duke University for our ELP technology pursuant to which we retain worldwide commercial rights to our product candidates. If approved in the United States, we intend to commercialize PB2452 independently and we may either commercialize PB1046 independently or in collaboration with a partner. As we advance towards regulatory approvals for our product candidates, we intend to establish a focused marketing and sales infrastructure. We may also explore collaborations or partnerships to commercialize PB2452 and PB1046 outside of the United States.

## Pipeline

Our clinical-stage pipeline is set forth below:

| Product Candidate | Indication | Mechanism of Action | Stage of Development | Worldwide Commercial Rights | Upcoming Milestones |
|---|---|---|---|---|---|
| PB2452 | Major Bleeding or Prior to Urgent Surgery in Patients on Ticagrelor | Reversal of the Antiplatelet Activity of Ticagrelor | **Phase 1** | PHASE Bio | **YE2018:** Phase 1 Full Data **1H2019:** Initiate Phase 2a and Report Data **2H2019:** Initiate Phase 2 Trial |
| PB1046 | Pulmonary Arterial Hypertension | VPAC2 Selective Agonist | **Phase 2b** | PHASE Bio | **1H2020:** Phase 2b Data |

### PB2452: Antiplatelet Therapy Reversal Agent for Ticagrelor

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

#### *Background on Acute Coronary Syndrome*

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

The primary treatment for ACS is the use of antiplatelet drugs to prevent the worsening of existing clots or to reduce the formation of additional clots. These clots can occur in the heart or in stents that are placed in the blocked coronary artery to keep the blood vessel open or elsewhere in the body. Without antiplatelet drugs, patients are at a significantly increased risk of recurrent heart attacks, stroke and death. The standard of care for ACS patients is dual antiplatelet therapy, or DAPT, which is a combination of aspirin and an inhibitor of a specific receptor found on platelets known as the $P2Y_{12}$ receptor. This combination is started after a patient experiences a heart attack or other manifestation of ACS and has been shown to significantly reduce platelet aggregation and clot formation and reduce the frequency of recurrent heart attacks, stroke and death.

While the antiplatelet drugs used in DAPT therapy have proven effective at improving overall outcomes in ACS patients, their suppression of blood clotting increases patients' risk of bleeding. Bleeding events in patients on antiplatelet therapy, which can occur spontaneously or as a result of injury or surgery, are classified as minor or major. In the 18,000-patient clinical trial, Platelet Inhibition and Patient Outcomes, or PLATO, conducted by AstraZeneca, ticagrelor was shown to be superior to the antiplatelet drug clopidogrel, marketed under the brand name Plavix, in reducing recurrent heart attack, stroke and death in patients with ACS. However, in both treatment groups, 11% to 12% of patients in the trial suffered major bleeding events, and in 5.8% of patients, these major bleeding events were fatal or life-threatening. The causes of bleeding varied in the trial population. In approximately 3% of the patients on ticagrelor, the major bleeding events were spontaneous and not related to any medical procedure, whereas approximately 9% of patients on ticagrelor developed major bleeding that was related to procedures like coronary artery bypass surgery, or CABG. Although the trial protocol recommended that patients who needed CABG stop taking ticagrelor for one to three days prior to surgery, nearly half of all

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

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

***Background on Antiplatelet Drugs***

The three oral antiplatelet $P2Y_{12}$ receptor antagonist drugs prescribed in DAPT therapy are clopidogrel, marketed under the brand name Plavix, prasugrel, marketed under the brand name Effient, and ticagrelor, marketed under the brand names Brilinta and Brilique. Unlike clopidogrel and prasugrel that permanently bind to and inhibit the target receptors on platelets, ticagrelor binds to the $P2Y_{12}$ receptor in a transient manner, quickly cycling on and off the receptor. We believe this transient binding of ticagrelor presents a unique opportunity to develop a specific reversal agent for ticagrelor, whereas the permanent binding of the other drugs to the receptor precludes a reversal agent from being developed.

Ticagrelor is considered the best-in-class $P2Y_{12}$ antiplatelet agent because it has demonstrated superior efficacy compared to clopidogrel. In 2017, ticagrelor accounted for 17% of new $P2Y_{12}$ antiplatelet prescriptions in the United States, with worldwide sales of over $1 billion, an increase of 29% over 2016 sales. Ticagrelor has achieved this level of market share despite the availability of generic versions of clopidogrel and prasugrel. We believe ticagrelor growth is being driven in part by treatment guidelines from the American College of Cardiology, American Heart Association and the European Society of Cardiology that recognize ticagrelor as the preferred antiplatelet treatment for ACS. We believe that the availability of a reversal agent could further drive the use of ticagrelor by making it the only reversible oral $P2Y_{12}$ antiplatelet treatment, thereby conferring a possible safety benefit over the other agents. Furthermore, based on the growth of clopidogrel prescriptions after the introduction of a generic form of that drug, we believe ticagrelor prescriptions could grow significantly after its patents expire and generic competition drives prices down to similar levels as other $P2Y_{12}$ antiplatelet therapies.

***Our Solution: PB2452***

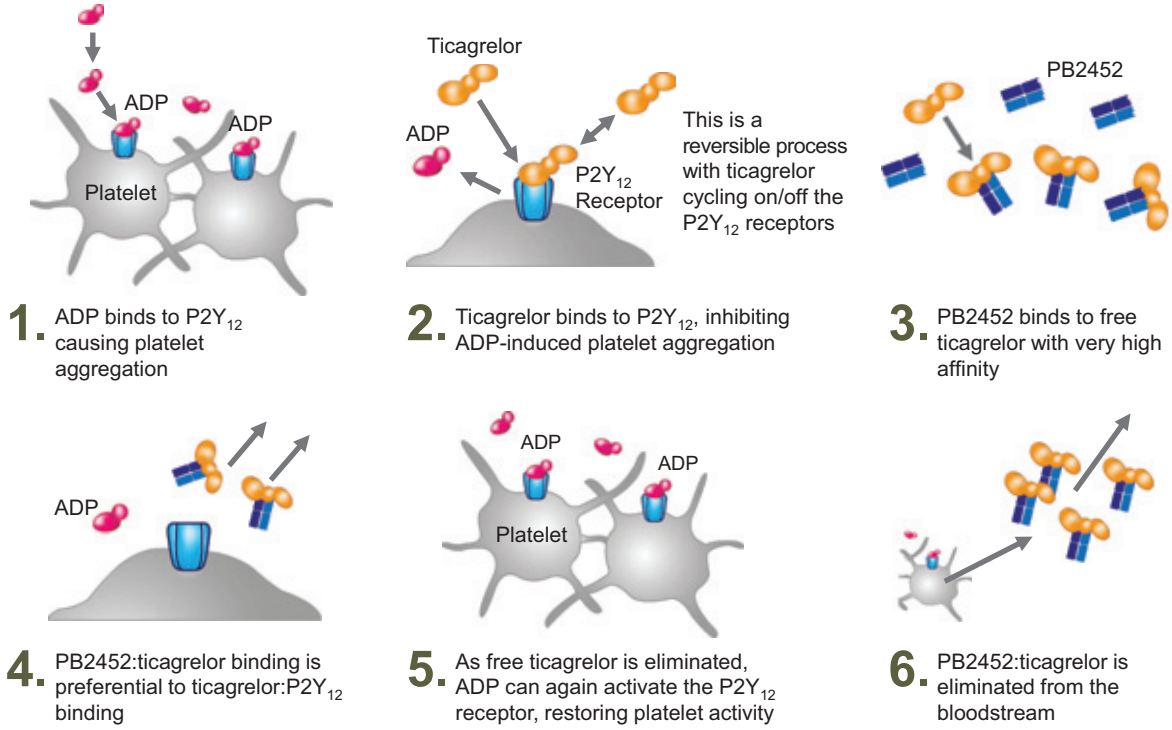
PB2452 is a human Fab fragment that binds to ticagrelor with high affinity and specificity to reverse ticagrelor's antiplatelet activity. We believe that the availability of PB2452 may further differentiate ticagrelor from other $P2Y_{12}$ receptor antagonists by providing for better clinical management of the balance between the desired antiplatelet effect and prevention or control of bleeding. We exclusively licensed PB2452 from MedImmune Limited, or MedImmune, a wholly owned subsidiary of AstraZeneca.

***PB2452 Background***

Ticagrelor works by binding to the $P2Y_{12}$ receptor on platelets, thereby preventing adenosine diphosphate, or ADP, from causing platelet aggregation. Ticagrelor binds transiently to the $P2Y_{12}$ receptor quickly cycling on and off, allowing PB2452 to bind to free ticagrelor, thereby preventing ticagrelor's activation of the receptor and

removing ticagrelor from circulation. With ticagrelor removed, ADP can once again bind the $P2Y_{12}$ receptor and induce platelet aggregation. This activity is illustrated below.

**Mechanism of action of ticagrelor and its reversal by PB2452**

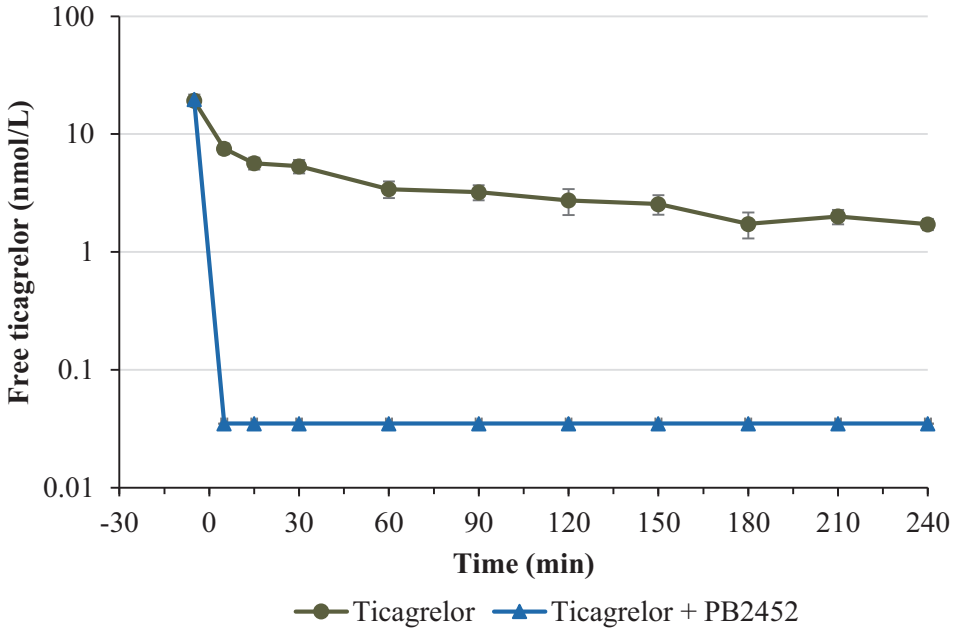



PB2452 binds to ticagrelor with an affinity that is 100 times stronger than ticagrelor's affinity for the $P2Y_{12}$ receptor. This high affinity enables PB2452 to bind to free ticagrelor, resulting in a rapid reversal of ticagrelor's effect and restoration of platelet activity.

***PB2452 Preclinical Studies***

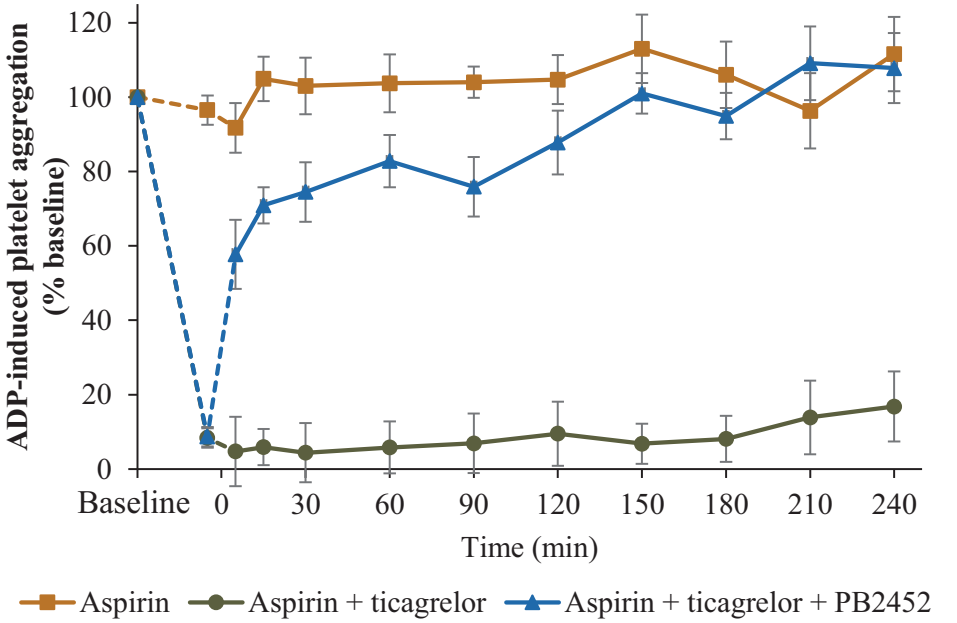
In preclinical studies conducted by AstraZeneca, it was observed that PB2452 rapidly removed free ticagrelor and restored normal platelet aggregation and normal bleeding time. In a preclinical model of pigs pre-dosed with ticagrelor and aspirin, circulating levels of ticagrelor dropped by over 100-fold when measured five minutes after the administration of PB2452 and remained below the limit of quantitation for at least four hours:

**Rapid removal of free ticagrelor from plasma in a pig model of PB2452**



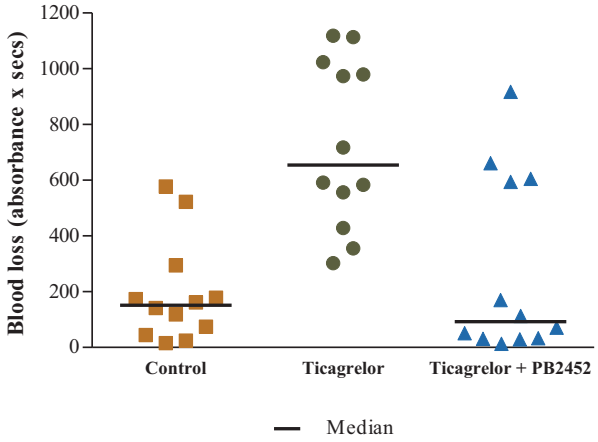

It was further observed in this model that dosing with ticagrelor and aspirin resulted in a 90% reduction in platelet aggregation. A single administration of PB2452 reversed and restored over 50% of ADP-induced platelet aggregation activity within five minutes and over 80% in one hour:

**Reversal of ticagrelor-treated platelet aggregation inhibition in a pig model of PB2452**



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

**Bleeding time in mice treated with ticagrelor in a mouse model of PB2452**




***Clinical Development of PB2452***

*Phase 1 Clinical Trial*

We recently completed a Phase 1 dose escalation clinical trial of PB2452, delivered as an intravenous infusion, in healthy subjects pre-dosed with ticagrelor that was designed to identify the target dose, determine proof of concept and evaluate the safety and tolerability of PB2452. We conducted this trial pursuant to an investigational new drug, or IND, application that we sponsored and that became effective in March 2018. We expect to report final data from this trial by the end of 2018.

Our Phase 1 clinical trial enrolled 72 subjects across 10 ascending dose cohorts. Based on pharmacokinetic and pharmacodynamic data from the early dose cohorts in the trial, we adjusted the intravenous infusion rate at different dose levels of PB2452 to identify the optimal dose and dosing regimen for future trials and for the target patient populations. The initial three cohorts of subjects were dosed with 30-minute intravenous infusions of PB2452 alone in order to assess pharmacokinetics and safety. Subsequent cohorts were pre-dosed with the standard clinical regimen of ticagrelor for three days prior to administration of PB2452 to enable direct assessment of reversal of ticagrelor's inhibition of platelet aggregation using platelet function assays. There were no PB2452-related AEs or SAEs in any of the dose cohorts.

In cohorts 5 and 6, which were the first cohorts in which we administered potentially pharmacodynamically active doses of PB2452, we saw rapid and complete reversal of ticagrelor's antiplatelet activity based upon restoration of platelet function. In 11 out of 12 subjects, platelet function was restored at the first measured time point at the end of the 30-minute infusion. The duration of reversal varied from approximately one to four hours depending upon the dose level and subject, with longer duration at higher doses. In cohort 7, we modified the dosing regimen to deliver a total dose of 18,000 mg, with 3,000 mg delivered in the first five minutes of infusion, followed by 15,000 mg delivered at a constant rate over an additional 7 hours and 55 minutes. In cohort 7, we observed that all subjects achieved complete and sustained reversal of platelet function within two hours after the start of infusion, with two out of six subjects showing complete reversal as rapidly as five minutes after the start of the infusion. On average, the duration of reversal in cohort 7 lasted approximately 16 hours from the start of the infusion as measured by restoration of platelet activity.

In cohorts 8, 9 and 10, we further refined the dose and dosing regimen of PB2452 in order to achieve both a more rapid onset of reversal compared to cohorts 5 and 6 and a longer duration of reversal compared to cohort 7. We administered a total dose of 18,000 mg, with 6,000 mg delivered in the first fifteen minutes of infusion in cohorts 8 and 9 and in the first ten minutes of infusion in cohort 10. Another 6,000 mg was administered after the initial infusion for a further three hours in cohorts 8 and 10, and for four hours in cohort 9. Each of the three cohorts then received a final 6,000 mg delivered for periods ranging from 8.75 hours to approximately 13 hours. In each of these cohorts, we observed both rapid and complete reversal within the first five minutes following initiation of infusion and a sustained duration of reversal of over 20 hours. We intend to further evaluate the dose and dosing regimens observed in cohorts 8, 9 and 10 in future clinical trials.

*Future Clinical Development Plans*

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

Upon completion of the Phase 2a clinical trial, we intend to request a meeting with the FDA to review the clinical profile of and confirm our development plans for PB2452. Subject to discussions with the FDA, in the second half of 2019 we intend to conduct a multi-center Phase 2 clinical trial in healthy older subjects aged 50 to 75 who have been pre-dosed with ticagrelor in order to assess the safety, tolerability and efficacy of the dose and dosing regimen of PB2452 established in our Phase 1 and Phase 2a clinical trials. Like the Phase 2a trial, these subjects will be enrolled in the Phase 2 trial because they resemble the patient population most likely to be treated with ticagrelor and potentially benefit from PB2452. The trial will be conducted with a pre-specified interim analysis after an initial subset of subjects has been treated with PB2452.

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

**PB1046 for the Treatment of Pulmonary Arterial Hypertension**

We are developing our second product candidate, PB1046, as a once-weekly novel treatment for PAH. PB1046 is based on our proprietary ELP half-life extension technology. We are currently conducting a Phase 2b clinical trial in PAH patients to assess the safety, tolerability and efficacy of PB1046. We have received two orphan drug designations for PB1046 from the FDA, one for the treatment of PAH and a second for cardiomyopathy associated with DMD. In February 2018, we received Small Business Innovation Research, or SBIR, grants from the National Institutes of Health in an aggregate amount of $2.8 million to support the clinical development of PB1046 for the treatment of PAH for the period from February 17, 2018 to July 31, 2020. In connection with the SBIR grants, the U.S. government will receive a non-exclusive, royalty-free license to use any technology we develop under such grants. As of June 30, 2018, we had not recognized or received any amounts under the SBIR grants.

***Background on PAH***

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

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

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

***Limitations of Current Therapies for PAH***

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

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

These drugs have been shown to improve exercise capacity, quality of life, pulmonary arterial pressure and short-term survival in PAH patients and suggest enhanced long-term survival based on observational studies. However, none of the current treatments is curative and long-term prognosis remains poor. These therapies have a singular approach to treating PAH by modulating the vasoconstrictive or vasodilatory pathways but have limited ability to address other disease processes such as inflammation, cell proliferation, fibrosis and vascular

remodeling. Furthermore, these drugs can cause hypotension, which can cause fainting and dizziness and can be life-threatening. As the disease progresses, additional vasodilator therapies are typically added to existing therapies rather than replacing drugs that are no longer providing sufficient benefit.

***Our Solution: PB1046***

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

***PB1046 Background***

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

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

***Clinical Development of PB1046***

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

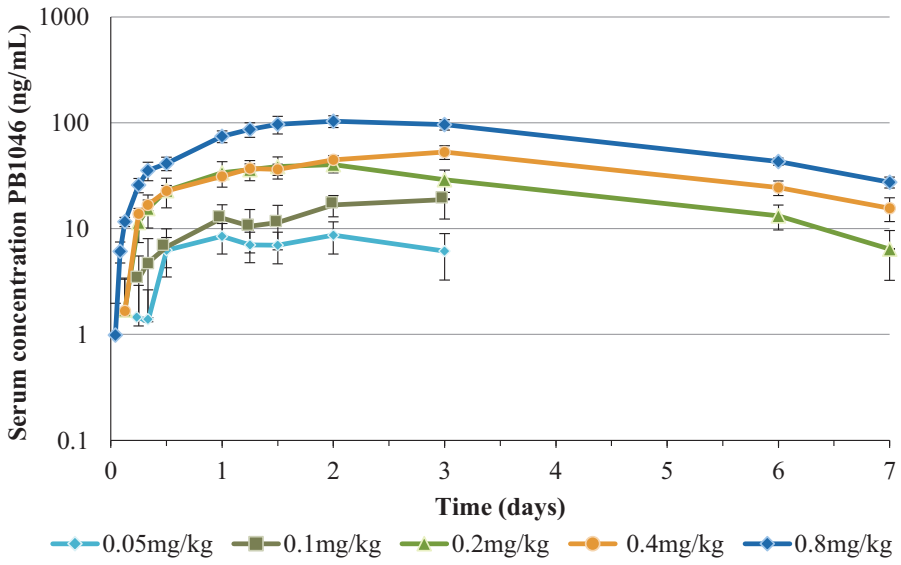
*PB1046 Phase 2b Clinical Trial*

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

*Phase 1 Single Ascending Dose Clinical Trial*

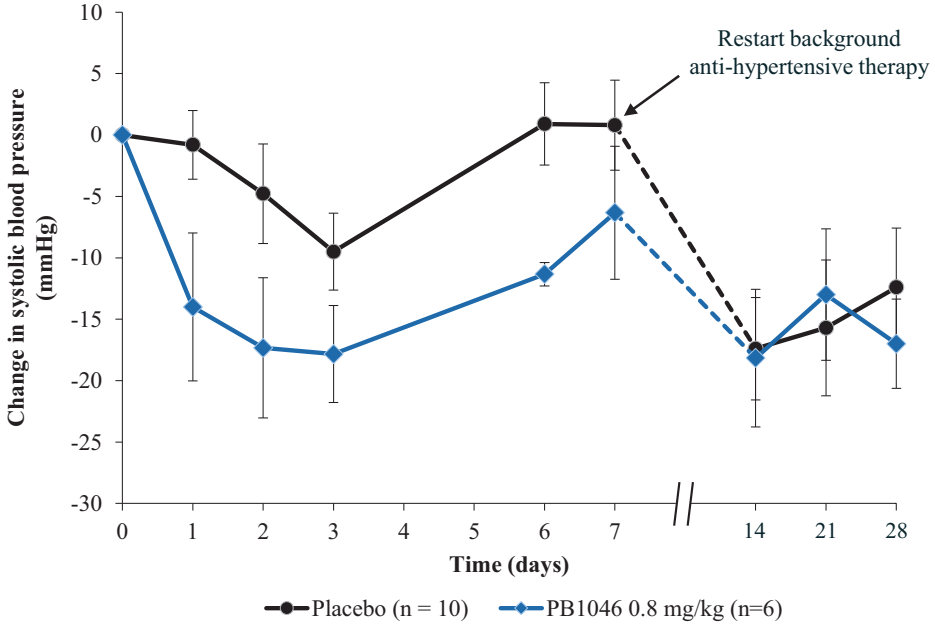
We have completed a single ascending dose Phase 1 clinical trial of subcutaneously injected PB1046 in 30 patients with hypertension to assess the safety and pharmacokinetics of PB1046 and to demonstrate early proof of concept. In this clinical trial, the patients stopped taking their standard of care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

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



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

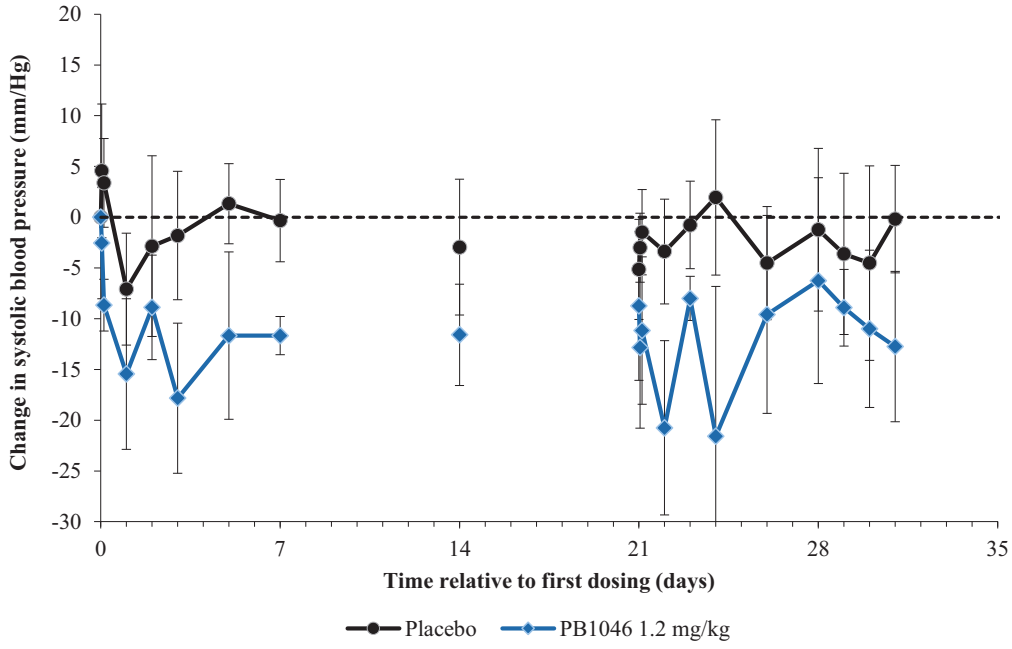
**Mean change in systolic blood pressure in a Phase 1 trial following single subcutaneous dose of PB1046**



*Phase 1b/2a Multiple Ascending Dose Clinical Trial*

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

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




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

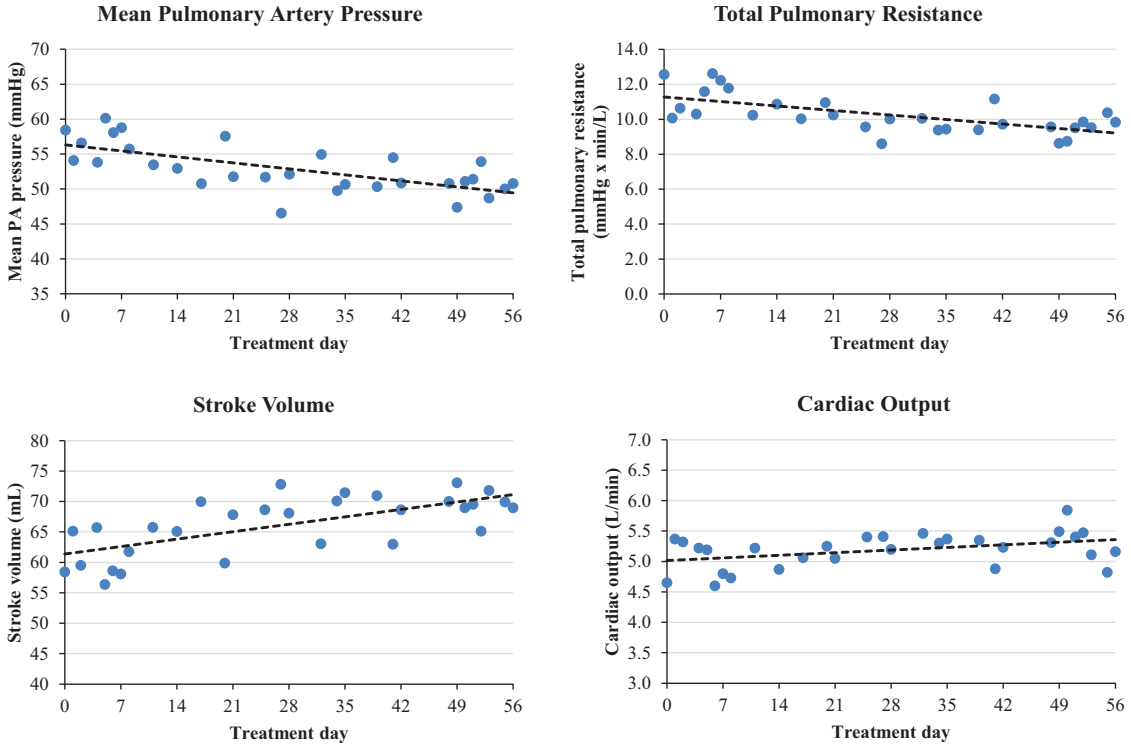
*Phase 1b/2a CardioMEMS Pilot Clinical Trial*

Prior to launching a large Phase 2b trial in patients with PAH, the FDA requested that we explore the safety and hemodynamics of PB1046 in patients with PAH. To achieve this objective, we initiated a pilot Phase 1b/2a

clinical trial in a small population of PAH patients who had an implanted CardioMEMS device. The patients enrolled in this trial were difficult-to-treat patients with long histories of PAH who were no longer responding to their current therapies. These patients initially received a dose of 0.2 mg/kg of PB1046, which was escalated weekly as tolerated and could be increased to a maximum dose of 2.0 mg/kg, while remaining on their existing therapies.

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

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




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

*Safety Overview from Clinical Trials of PB1046*

There were no drug-related SAEs reported for any of the patients who have received PB1046. When PB1046 was administered subcutaneously, it was almost always associated with a mild- to moderate-injection site erythema, or patch of redness, which on average appeared at about 12 hours after injection. The injection site erythema was not judged by the investigator to be an allergic type reaction; rather, in the investigator's view, it

was likely to be associated with the activity of VIP binding to receptors in the skin, resulting in local vasodilation. Additionally, 70% of patients receiving a subcutaneous injection of PB1046 experienced mild pain or tenderness at the injection site, which occurred hours to days after injection and on average lasted about one week. One-third of the patients also experienced mild pruritus, or itching, at the site of injection. We believe that these events are primarily due to the fused VIP peptide since similar events were not observed in clinical trials of other constructs that contain the ELP domain. None of the injection site reactions were judged to be serious. We have also completed a Phase 1 clinical trial with intravenously administered PB1046 in which we observed a similar tolerability profile. Notably, there were no events of symptomatic hypotension related to PB1046 in any of the subjects who have received PB1046.

*Preclinical Studies*

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

***Potential applications of PB1046 in other indications***

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

- ***DMD-associated Cardiomyopathy***. Cardiac dysfunction is a very common manifestation of DMD and a common cause of death for individuals with this condition. The ability of PB1046 to increase contractibility of cardiac muscles presents the possibility that it could provide therapeutic benefit to these patients. We observed that PB1046 slowed deterioration in cardiac function and preserved skeletal muscle function in a mouse model of DMD. In addition to direct effects on cardiac function, we believe decreased fibrosis also contributed to the positive effects of PB1046 on both cardiac and skeletal muscle in this model.

- ***Cystic Fibrosis***. VIP has been shown to stimulate the processing of cystic fibrosis transmembrane regulator, or CFTR, the protein defective in patients with cystic fibrosis, or CF. In mice lacking the gene for VIP, CFTR is not located at the cell surface, where it is required to function properly, but accumulates within the cell. These mice have lung abnormalities that resemble CF and treatment with VIP peptide restored CFTR to the cell surface and corrected the lung tissue abnormalities. Treatment of human epithelial cells containing the most common CFTR mutation found in patients with CF, F508del, with PB1046 has been observed to increase CFTR activity, providing further support that PB1046 may have potential as a treatment for patients with CF.

**ELP Technology**

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

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

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

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

***Preclinical Programs***

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

Our more advanced preclinical programs include:

- ***C-type natriuretic peptide***. C-type natriuretic peptide, or CNP, is a regulator of bone growth and can rescue defects in fibroblast growth factor 3 that cause achondroplasia resulting in dwarfism. Native CNP has a half-life of less than three minutes, limiting its use as a direct therapeutic. We are developing our CNP-ELP product candidate to deliver therapeutic levels of CNP with once weekly subcutaneous injections. In a mouse model, we observed a demonstrated effect on linear growth when our CNP-ELP product candidate was injected once every four days.

- ***Glucagon-like peptide-2***. Glucagon-like peptide-2, or GLP-2, stimulates growth of intestinal villi, increasing their ability to absorb nutrients. GLP-2 is a potential treatment for patients with short bowel syndrome, Crohn's disease or mucositis in patients undergoing cancer treatment. Teduglutide, currently marketed under the brand name Gattex, is an FDA-approved therapy based on GLP-2 that requires daily injections. In animal models, our GLP-2-ELP product candidate provided sustained levels of GLP-2, resulting in greater efficacy than teduglutide with less frequent dosing.

**License Agreements**

***MedImmune Limited***

In November 2017, we entered into an exclusive license agreement with MedImmune, a wholly owned subsidiary of AstraZeneca, or the MedImmune License. Pursuant to the MedImmune License, MedImmune granted us an exclusive, worldwide license under certain patent rights owned or controlled by MedImmune to develop and commercialize any products covered by the MedImmune License, or the MedImmune licensed products, for the treatment, palliation, diagnosis or prevention of any human disorder or condition. The in-licensed patent rights are generally directed to antibodies that bind to ticagrelor and methods of use and include one issued patent in the United States, three pending patent applications in the United States and 12 pending foreign applications. The last patent is expected to expire in 2036 without extension. We have the right to sublicense the licensed technology to third parties subject to certain conditions as specified in the MedImmune

License. Under the MedImmune License, we grant to MedImmune a worldwide, non-exclusive, royalty-free, irrevocable license and right of reference solely to exploit any drug product containing ticagrelor or any invention, discovery, development or modification with respect to any drug product containing ticagrelor.

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

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

As of June 30, 2018, we have paid $0.6 million under the MedImmune License, including $0.5 million in third-party storage costs.

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

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

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

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

***Duke University***

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

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

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

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

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

As of June 30, 2018, we have not paid any amounts under the Duke License. As of May 2017, Duke is required to pay us a percentage of revenue that it receives from granting a license or sublicense with respect to certain products covered under the Duke License. As of June 30, 2018, Duke has not paid us any of such fees. We also must pay Duke the first $1.0 million of non-royalty payments we receive from a sublicensee, and thereafter a low double-digit percentage of any additional non-royalty payments we receive.

The Duke License requires us to use commercially reasonable efforts to develop, obtain and maintain regulatory approval for and commercialize the Duke licensed products according to a particular development schedule throughout the term of the Duke License. We are required to apply for, prosecute and maintain all U.S. and foreign patent rights under the Duke License. As of June 30, 2018, we have incurred $1.0 million in patent legal fees. In addition, our rights under the Duke License are not assignable without the prior written consent of Duke, except to a third party acquirer by our merger or sale of our stock or assets, or to an affiliate of our company.

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

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

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

**Manufacturing**

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

***PB2452***

To date, we have used PB2452 provided to us pursuant to the MedImmune License for our Phase 1 clinical trial. The PB2452 drug substance was manufactured by Wacker Biotech GmbH, a third party contract manufacturer, utilizing Wacker's proprietary *E. coli* strain. Development and scale-up of a more efficient manufacturing process is currently in process. This optimized process will be used for the manufacture of future clinical development drug supply and, if PB2452 is approved, commercial supply. As we advance PB2452 through clinical development, we intend to establish additional supply agreements for the manufacture of PB2452 in order to meet our expected needs for potential commercial demand.

***PB1046 and our ELP Preclinical Pipeline***

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

**Sales and Marketing**

We retain worldwide commercial rights to all of our product candidates. Given our stage of development, we have not yet established a commercial organization or distribution capabilities. We intend to commercialize

PB2452, if approved, independently in the United States because we believe the patient populations and medical specialists for this indications are sufficiently concentrated to allow us to effectively promote these products with a targeted sales team. We may explore, and selectively pursue, strategic collaborations or partnerships with third parties to commercialize PB1046, if approved, in the United States and any approved products outside of the United States in order to maximize the commercial potential of our products.

**Competition**

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

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

***PB2452***

There are currently no known reversal agents approved or in clinical development for ticagrelor. As a result, market acceptance of PB2452, if approved, will depend heavily on the continued market acceptance and use of ticagrelor. Ticagrelor competes against other commercially available antiplatelet therapies, including other $P2Y_{12}$ receptor antagonists, many of which are available as generic drugs and therefore currently significantly less expensive than ticagrelor. New antiplatelet therapies may also be developed in the future, including other reversible $P2Y_{12}$ receptor antagonists and other antiplatelet therapies, which could also have reversal agents, that could displace ticagrelor as the preferred antiplatelet agent for ACS.

***PB1046***

Although we anticipate that PB1046 may be used as a complement to patients' existing therapies, we expect to compete with existing treatments for PAH patients with class II through class IV symptoms that target the endothelin, nitric oxide and prostacyclin pathways, as well as any generic equivalents that may be developed, 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, including:

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

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

**Intellectual Property**

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

The term of individual patents varies depending on the date of filing of the patent application and the legal term of patents in the countries in which they are obtained. Generally, patents issued from regularly filed applications in the United States are granted a term of 20 years from the earliest filing date of a non-provisional application. In addition, in certain instances, a patent term can be adjusted to recapture a portion of the delay by the United States Patent and Trademark Office in issuing the patent. In addition, a patent term may be extended to recapture a portion of the patent term effectively lost as a result of the FDA regulatory review period of the drug covered by the patent. The patent term extension based upon delay by the FDA can be up to five years beyond the expiration of the patent, but cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and the extension may only apply to one patent that covers the approved drug (and to only those patent claims covering the approved drug or a method for using it). There can be no assurance that any such patent term adjustment or extension will be obtained. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically in countries that we file, the patent term is 20 years from the earliest filing date of a non-provisional patent application. However, the actual protection afforded by a patent varies on a product-by-product basis, from country to country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

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

As of September 30, 2018, our patent estate contained at least 15 patent families that we own or in-license which protects various aspects of our ELP technology or our product candidates. We own or have rights in 20

United States patents, over 10 United States patent applications, over 50 foreign patents and over 40 foreign patent applications.

***PB2452***

With regard to PB2452, we in-license one patent family. As of September 30, 2018, this patent family includes one issued U.S. patent with composition of matter claims covering PB2452 that is scheduled to expire in 2036 without taking patent term extensions into account, five pending U.S. patent applications and 12 pending foreign applications, that if issued, would expire in 2035. We are heavily dependent on the patented or proprietary technologies that we license from third parties.

***PB1046***

As of September 30, 2018, our portfolio of owned and in-licensed patents and patent applications relating to PB1046 consists of six issued patents in the United States, five pending applications in the United States, 16 granted foreign patents and 19 pending foreign applications with claims directed to compositions of matter covering PB1046 and methods of use thereof, including use in PAH, cystic fibrosis and cardiomyopathy associated with DMD, that we expect to expire between 2027 and 2036, without taking patent term extensions into account

***ELP Technology***

As of September 30, 2018, we owned two patent families relating to our ELP technology, which consists of one granted patent in the United States, one pending application in the United States and six pending foreign applications. The granted patent expires in 2021 without taking patent term extensions into account.

**Government Regulation and Product Approval**

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

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

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

- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with cGMP and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency and of selected clinical investigation sites to assess compliance with Good Clinical Practices, or GCP; and

- FDA review and approval of the BLA to permit commercial marketing of the product for particular indications for use in the United States.

***Preclinical and Clinical Development***

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

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

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

- Phase 1—The investigational product is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses and, if possible, to gain early evidence on effectiveness.

- Phase 2—The investigational product is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.

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

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

***BLA Submission and Review***

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

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

After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response letter will describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the Complete Response letter without first conducting required inspections, testing submitted product lots and/or reviewing proposed labeling. In issuing the Complete Response letter, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification. The FDA may delay or

refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

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

***Accelerated Approval Program***

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

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

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

***Orphan Drug Designation***

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

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusive approval (or exclusivity),

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

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

***Breakthrough Therapy Designation***

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

***Post-Approval Requirements***

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

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including AEs of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of a product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical studies;

- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of existing product approvals;
- product seizure or detention, or refusal of the FDA to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

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

***Biosimilars and Reference Product Exclusivity***

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

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

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

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

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

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

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

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

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

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations, impose certain requirements relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization on certain health plans, healthcare clearinghouses and certain healthcare providers, known as covered entities, and their respective business associates, independent contractors that perform certain services involving the use or disclosure of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates and

gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorneys' fees and costs associated with pursuing federal civil actions.

The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to payments or other transfers of value made to physicians and teaching hospitals and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians and their immediate family members.

We may also be subject to state and foreign law equivalents of each of the above federal laws; state laws that require manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or that otherwise restrict payments that may be made to healthcare providers; state and local laws that require the registration of pharmaceutical sales representatives; as well as state and foreign laws that govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm and the curtailment or restructuring of our operations. To the extent that any of our products are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

***Coverage and Reimbursement***

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

provide coverage for a drug product does not assure that other payors will also provide coverage and adequate reimbursement.

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

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

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

***Impact of Healthcare Reform on our Business***

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

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. In March 2010, the ACA was passed, which substantially changed the way healthcare is financed by both the government and private insurers and significantly impacts the U.S. pharmaceutical industry. The ACA, among other things: (1) increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations; (2) 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; (3) expanded the availability of lower pricing under the 340B drug pricing program by adding new entities to the program; (4) 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; (5) expanded the eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals, thereby potentially increasing manufacturers' Medicaid rebate liability; (6) 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 (7) established a Center for Medicare 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 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." More recently, in July 2018, CMS announced that it is suspending further collections and payments to and from certain ACA-qualified health plans and health insurance issuers under the ACA risk adjustment program pending the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment.

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

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

## Employees

As of September 30, 2018, we had 18 full-time employees. All of our employees are located in the United States. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

## Facilities

We operate in an approximately 16,000 square foot facility in Malvern, Pennsylvania pursuant to a lease agreement that expires in September 2023. We also lease office space in San Diego, California pursuant to a month-to-month lease agreement. We believe that our existing facilities are suitable and adequate to meet our current needs. We intend to add new facilities or expand existing facilities as we add employees, and we believe that suitable additional or substitute space will be available as needed to accommodate any such expansion of our operations.

## 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.

## MANAGEMENT

### Executive Officers and Directors

The following table sets forth certain information with respect to our executive officers and directors, including their ages as of September 15, 2018:

| Name | Age | Position(s) |
|---|---|---|
| ***Executive Officers*** | | |
| Jonathan P. Mow | 53 | Chief Executive Officer and Director |
| John Sharp | 53 | Chief Financial Officer |
| Susan Arnold, Ph.D. | 43 | Vice President, Preclinical and Chemistry, Manufacturing and Controls |
| James Ballance, Ph.D. | 59 | Vice President, Research and Scientific Affairs |
| John Lee, M.D., Ph.D. | 50 | Chief Medical Officer |
| Michael York | 53 | Vice President, Corporate Development and Commercial Strategy |
| ***Non-Employee Directors*** | | |
| Clay B. Thorp[(1)(2)] | 51 | Chairman |
| Nancy J. Hutson, Ph.D.[(1)(2)] | 69 | Director |
| Peter Justin Klein, M.D., J.D.[(1)] | 41 | Director |
| Caroline Loewy[(3)] | 51 | Director |
| Bibhash Mukhopadhyay, Ph.D.[(2)(3)] | 37 | Director |
| Linda Tufts[(3)] | 64 | Director |
| Tyrell Rivers, Ph.D.[(4)] | 45 | Director |

(1) Member of compensation committee.
(2) Member of nominating and corporate governance committee.
(3) Member of audit committee.
(4) Dr. Rivers will resign from our board of directors prior to the completion of this offering.

#### *Executive Officers*

*Jonathan P. Mow* has served as our Chief Executive Officer and a member of our board of directors since September 2014. He previously served as our Chief Business Officer from December 2012 to September 2014. Mr. Mow received a B.S. in mechanical engineering from the University of California, Berkeley and a M.B.A. from Carnegie Mellon University. Our board of directors believes that Mr. Mow is qualified to serve as a director based on his role as our Chief Executive Officer and his extensive management experience in the pharmaceutical industry.

*John Sharp* has served as our Chief Financial Officer since April 2016. Prior to joining our company, Mr. Sharp served as chief financial officer of HUYA Bioscience International, LLC, a biopharmaceutical company, from March 2014 to December 2015. From April 2007 to February 2014, Mr. Sharp served as chief financial officer of Ligand Pharmaceuticals, Inc., a biopharmaceutical company. Mr. Sharp received a B.S. in business administration from San Diego State University and is a certified public accountant.

*Susan Arnold* has served as our Vice President of Preclinical and Chemistry, Manufacturing and Controls since October 2010. Dr. Arnold received a B.A. in biology from Holy Family University and a M.S. in cell biology and biotechnology and a Ph.D. in cell and molecular biology from the University of the Sciences in Philadelphia.

*James Ballance* has served as our Vice President of Research and Scientific Affairs since October 2014. He previously served as our Vice President of Scientific Affairs from January 2013 to October 2014. Dr. Ballance received a B.Sc. in applied biology from the University of Wales and a Ph.D. in fungal molecular genetics from the University of Bristol.

*John Lee* has served as our Chief Medical Officer since April 2016. Prior to joining our company, Dr. Lee served as the vice president and global head of the Cardiovascular Center of Excellence at Quintiles Transnational Corp., a pharmaceutical outsourcing services company, from January 2015 to April 2016. He previously served in various roles at Bristol-Myers Squibb, most recently as executive director, head of the cardiovascular/metabolic therapeutic area from January 2010 to December 2014. Dr. Lee received a B.A. in biological sciences from Harvard University and a M.D. and a Ph.D. in biochemistry from Boston University.

*Michael York* has served as our Vice President of Corporate Development and Commercial Strategy since June 2018. Prior to joining our company, Mr. York served as the vice president of global business development and alliance management of Orexigen Therapeutics, Inc., a biopharmaceutical company, from August 2015 to June 2018. He previously served as a senior advisor for MKO Global Partners, L.P., a biopharmaceutical strategic advisory firm, from January 2015 to August 2015. From July 2013 to December 2014, Mr. York served as president and chief executive officer of Sente, Inc., a cosmeceutical company. Mr. York received a B.A. in public administration and economics from San Diego State University and a M.B.A. from the University of Redlands.

***Non-Employee Directors***

*Clay B. Thorp* co-founded our company in 2002 and has served as a member of our board of directors since that time. Mr. Thorp has served as chairman of our board of directors since November 2014. In 2001, Mr. Thorp co-founded and has since served as general partner of Hatteras Venture Partners, an investment firm, where he leads investments in a range of life science companies in the biopharmaceutical, medical device, diagnostics and research informatics sectors. He has served on the board of directors of Clearside Biomedical, Inc. since January 2012. Previously, he helped found several life sciences companies, including serving as co-founder, chief executive officer and chairman of Synthematix, Inc., a chemistry informatics company that was acquired by Symyx Technologies in 2005, co-founder and head of corporate development for Novalon Pharmaceutical Corporation, which was sold to Karo Bio in 2000, and co-founder and president of Xanthon, Inc., a bioinformatics company with electro-chemical detection technology for direct analysis of DNA, RNA and proteins. Mr. Thorp received a B.A. in mathematics and history from the University of North Carolina at Chapel Hill and a Masters of Public Policy from Harvard University. Our board of directors believes that Mr. Thorp is qualified to serve as a director based on his institutional knowledge of our company and his experience as an entrepreneur and an investor in life sciences companies.

*Nancy J. Hutson* has served as a member of our board of directors since March 2018. Dr. Hutson retired in 2006 as the senior vice president of global research and development at Pfizer, Inc. Dr. Hutson has served on the boards of directors of BioCryst Pharmaceuticals, Inc. since January 2012 and Endo International plc, a pharmaceutical company, since February 2014. Dr. Hutson previously served on the board of directors of Cubist Pharmaceuticals, Inc., a biopharmaceutical company, from January 2008 until it was acquired by Merck & Co., Inc. in December 2014. Dr. Hutson received a B.A. in general biology from Illinois Wesleyan University and a Ph.D. in physiology and biochemistry from Vanderbilt University. Our board of directors believes that Dr. Hutson is qualified to serve as a director based on her 30 years of experience in the pharmaceutical industry and her extensive experience in drug research and development.

*Peter Justin Klein* has served as a member of our board of directors since December 2009. Dr. Klein currently serves as a partner at New Enterprise Associates, Inc., a venture capital firm, a position he has held since February 2012. He has served on the board of directors of Senseonics Holdings, Inc., a medical technology company, since December 2015. Dr. Klein received an A.B. in economics and a B.S. in biological anthropology and anatomy from Duke University, a J.D. from Harvard Law School and a M.D. from Duke University. Our board of directors believes that Dr. Klein is qualified to serve as a director based on his extensive experience in the healthcare industry.

*Caroline Loewy* has been a member of our board of directors since July 2018. Ms. Loewy is a consultant providing strategic advisory services for biopharmaceutical companies, a position she has held since February 2014. She was a co-founder and served as the chief business officer and chief financial officer at Achieve Life

Sciences from September 2015 to August 2017, when it was acquired by OncoGenex Pharmaceuticals, Inc. Ms. Loewy previously served as the chief financial officer at Tobira Therapeutics from September 2012 to February 2014. Ms. Loewy has served as a member of the boards of directors of CymaBay Therapeutics since December 2016 and Aptose Biosciences since April 2018. Ms. Loewy received a B.A. from the University of California, Berkeley, and a M.B.A./M.S. from Carnegie Mellon University. Our board of directors believes that Ms. Loewy is qualified to serve as a director based on her financial expertise as a former chief financial officer as well as her extensive experience in the biopharmaceutical industry.

*Bibhash Mukhopadhyay* has served as a member of our board of directors since February 2018. Dr. Mukhopadhyay currently serves as a principal at New Enterprise Associates, Inc., a position he has held since October 2015. Previously, Dr. Mukhopadhyay was an associate director of business development at MedImmune, LLC, the research and development subsidiary of AstraZeneca, from December 2013 to September 2015. Prior to that time, he served as a manager for Johnson & Johnson from October 2010 to November 2013. Dr. Mukhopadhyay received a B.S. in biochemistry and molecular biology from the All India Institute of Medical Sciences, a M.S. in neuroscience from Georg-August-Universität Göttingen and a Ph.D. in biomedical sciences from Baylor College of Medicine. Our board of directors believes that Dr. Mukhopadhyay is qualified to serve as a director based on his extensive experience in the healthcare industry, including in drug research and development.

*Tyrell Rivers* has served as a member of our board of directors since May 2018. Dr. Rivers currently serves as an executive director of the corporate development group of AstraZeneca, a position he has held since May 2014. Prior to that time, Dr. Rivers served as a senior associate at MedImmune Ventures from October 2009 to May 2014. He served on the board of directors of G1 Therapeutics, Inc., a clinical-stage biopharmaceutical company, from March 2017 to June 2018. Dr. Rivers received a B.S. in chemical engineering from the Massachusetts Institute of Technology, a Ph.D. from the University of Texas at Austin and a M.B.A. from New York University. Dr. Rivers has advised us that he will resign from our board of directors prior to the completion of this offering.

*Linda Tufts* has served as a member of our board of directors since March 2018. Ms. Tufts has served as a general partner of Fletcher Spaght, Inc., a consulting firm for healthcare and technology companies, since 1989. She also serves as the general partner of Fletcher Spaght Ventures, Fletcher Spaght Inc.'s venture capital affiliate, a position she has held since 2001. Ms. Tufts received an S.B. in humanities and science and in electrical engineering from the Massachusetts Institute of Technology and an S.M in management (finance) from the Sloan School of Management at the Massachusetts Institute of Technology. Our board of directors believes that Ms. Tufts is qualified to serve as a director based on her extensive experience consulting in the healthcare and life sciences sectors.

**Family Relationships**

There are no family relationships among any of our executive officers or directors.

**Board Composition**

Our board of directors currently consists of eight members. All of our directors currently serve on the board of directors pursuant to voting rights granted by our current amended and restated certificate of incorporation, which entitles (1) holders of a majority of the outstanding shares of common stock to elect one director, which is currently Jonathan P. Mow; (2) holders of a majority of the outstanding shares of Series 1 redeemable convertible preferred stock to elect one director, which is currently Clay B. Thorp; (3) entities affiliated with Fletcher Spaght Ventures to elect one director, which is currently Linda Tufts; (4) New Enterprise Associates to elect one director, which is currently Peter Justin Klein; (5) Zeneca to elect one director, which is currently Tyrell Rivers; (6) holders of a majority of the outstanding shares of our Series D redeemable convertible preferred stock to elect one director, which is currently Bibhash Mukhopadhyay; and (7) holders of a majority of the outstanding shares of our common and preferred stock, voting together as a single class on an as-converted basis to elect two directors, which are Nancy Hutson and Caroline Loewy. Such voting rights will expire upon the closing of this

offering. Upon the termination of these provisions, there will be no further contractual rights or obligations regarding the nomination or election of our directors. Thereafter, each of our current directors will continue to serve until the election and qualification of his or her successor, or his or her earlier death, resignation or removal.

In accordance with the terms of our amended and restated certificate of incorporation and amended and restated bylaws, which will be effective following the closing of this offering, our board of directors will consist of seven directors and will be divided into three classes, Class I, Class II and Class III, with members of each class serving staggered three-year terms. At each annual meeting of stockholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. Effective upon the closing of this offering, our board of directors will be divided into the following classes:

- Class I, which will consist of Peter Justin Klein and Linda Tufts, whose terms will expire at our first annual meeting of stockholders to be held after the closing of this offering;
- Class II, which will consist of Clay B. Thorp and Jonathan P. Mow, whose terms will expire at our second annual meeting of stockholders to be held after the closing of this offering; and
- Class III, which will consist of Nancy J. Hutson, Caroline Loewy and Bibhash Mukhopadhyay, whose terms will expire at our third annual meeting of stockholders to be held after the closing of this offering.

Our amended and restated bylaws, which will become effective upon the closing of this offering, will provide that the authorized number of directors may be changed only by resolution approved by a majority of our board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors.

The division of our board of directors into three classes with staggered three-year terms may delay or prevent a change of our management or a change of control.

**Director Independence**

Our board of directors has undertaken a review of the independence of the directors and considered whether any director has a material relationship with us that could compromise his ability to exercise independent judgment in carrying out his responsibilities. Based upon information requested from and provided by each director concerning such director's background, employment and affiliations, including family relationships, our board of directors determined that Clay B. Thorp, Nancy J. Hutson, Peter Justin Klein, Caroline Loewy, Bibhash Mukhopadhyay and Linda Tufts, representing six of our seven continuing directors, are "independent directors" as defined under current rules and regulations of the SEC and the listing standards of The Nasdaq Stock Market LLC, or Nasdaq. In making these determinations, our board of directors considered the current and prior relationships that each non-employee director has with our company and all other facts and circumstances that our board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director and the transactions involving them described in "Certain Relationships and Related Party Transactions."

**Board Committees**

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

***Audit Committee***

Upon the closing of this offering, our audit committee will consist of three directors, Caroline Loewy, Bibhash Mukhopadhyay and Linda Tufts, each of whom our board of directors has determined satisfies the

independence requirements for audit committee members under the listing standards of Nasdaq and Rule 10A-3 of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Each member of our audit committee meets the financial literacy requirements under the rules and regulations of Nasdaq and the SEC. Caroline Loewy is the chairman of the audit committee and our board of directors has determined that she is an audit committee "financial expert" as defined by Item 407(d) of Regulation S-K under the Securities Act. The principal duties and responsibilities of our audit committee include, among other things:

- selecting a qualified firm to serve as the independent registered public accounting firm to audit our financial statements;
- helping to ensure the independence and performance of the independent registered public accounting firm;
- discussing the scope and results of the audit with the independent registered public accounting firm, and reviewing, with management and the independent accountants, our interim and year-end operating results;
- developing procedures for employees to submit concerns anonymously about questionable accounting or audit matters;
- reviewing our policies on risk assessment and risk management;
- reviewing related party transactions;
- obtaining and reviewing a report by the independent registered public accounting firm at least annually, that describes its internal quality-control procedures, any material issues with such procedures, and any steps taken to deal with such issues when required by applicable law; and
- approving (or, as permitted, pre-approving) all audit and all permissible non-audit services, other than de minimis non-audit services, to be performed by the independent registered public accounting firm.

Our audit committee will operate under a written charter, to be effective immediately prior to the closing of this offering that satisfies the applicable rules of the SEC and the listing standards of Nasdaq.

***Compensation Committee***

Upon the closing of this offering, our compensation committee will consist of three directors, Nancy J. Hutson, Peter Justin Klein and Clay B. Thorp. Our board of directors has determined that each of the compensation committee members is a non-employee member of our board of directors as defined in Rule 16b-3 under the Exchange Act. Nancy J. Hutson will be the chairman of the compensation committee. The composition of our compensation committee meets the requirements for independence under the current listing standards of Nasdaq and current SEC rules and regulations. The principal duties and responsibilities of our compensation committee include, among other things:

- reviewing and approving, or recommending that our board of directors approve, the compensation of our executive officers;
- reviewing and recommending to our board of directors the compensation of our directors;
- reviewing and approving, or recommending that our board of directors approve, the terms of compensatory arrangements with our executive officers;
- administering our stock and equity incentive plans;
- reviewing and approving, or recommending that our board of directors approve, incentive compensation and equity plans; and

- reviewing and establishing general policies relating to compensation and benefits of our employees and reviewing our overall compensation philosophy.

Our compensation committee will operate under a written charter, to be effective immediately prior to the closing of this offering, that satisfies the applicable rules of the SEC and the listing standards of Nasdaq.

***Nominating and Corporate Governance Committee***

Upon the closing of this offering, our nominating and corporate governance committee will consist of three directors, Nancy J. Hutson, Peter Justin Klein and Clay B. Thorp. Clay B. Thorp will be the chairman of the nominating and corporate governance committee. The composition of our nominating and governance committee meets the requirements for independence under the current listing standards of Nasdaq and current SEC rules and regulations. The nominating and corporate governance committee's responsibilities include, among other things:

- identifying, evaluating and selecting, or recommending that our board of directors approve, nominees for election to our board of directors and its committees;
- evaluating the performance of our board of directors;
- considering and making recommendations to our board of directors regarding the composition of our board of directors and its committees;
- reviewing developments in corporate governance practices;
- evaluating the adequacy of our corporate governance practices;
- developing and making recommendations to our board of directors regarding corporate governance guidelines and matters; and
- overseeing an annual evaluation of our board of directors' performance.

Our nominating and governance committee will operate under a written charter, to be effective immediately prior to the closing of this offering, that satisfies the applicable rules of the SEC and the listing standards of Nasdaq.

**Compensation Committee Interlocks and Insider Participation**

None of our executive officers currently serves, or in the past year has served, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving on our board of directors or compensation committee. None of the members of our compensation committee is an officer or employee of our company, nor have they ever been an officer or employee of our company.

**Code of Business Conduct and Ethics**

In connection with this offering, we have adopted a Code of Business Conduct and Ethics, or the Code of Conduct, applicable to all of our employees, executive officers and directors. Following the closing of this offering, the Code of Conduct will be available on our website at www.phasebio.com. The nominating and corporate governance committee of our board of directors will be responsible for overseeing the Code of Conduct and must approve any waivers of the Code of Conduct for employees, executive officers and directors. We expect that any amendments to the Code of Conduct, or any waivers of its requirements, will be disclosed on our website as required by applicable law or the listing standards of Nasdaq. The inclusion of our website address in this prospectus does not include or incorporate by reference into this prospectus the information on or accessible through our website.

**Non-Employee Director Compensation**

In the year ended December 31, 2017, we did not pay any fees to, make any equity awards or non-equity awards to, or pay any other compensation to the non-employee members of our board of directors for their services as directors. Our non-employee directors only received reimbursement of their actual out-of-pocket costs and expenses incurred in connection with attending board meetings. Jonathan P. Mow, our Chief Executive Officer, is also a member of our board of directors, but did not receive any additional compensation for his service as a director.

As of December 31, 2017, Ashutosh Chilkoti held 9,038 shares of common stock underlying outstanding option grants. Dr. Chilkoti resigned from our board of directors effective August 27, 2018.

On August 8, 2018, we granted options to purchase 9,038 shares to Nancy Hutson and 36,155 shares to Caroline Loewy, each at an exercise price of $4.65 per share, with 25% of the shares subject to such option vesting on July 19, 2019, with respect to Ms. Loewy's award, and on July 27, 2019, with respect to Dr. Hutson's award, and the remaining shares vesting in equal monthly installments over 36 months.

**Non-Employee Director Compensation Policy**

In anticipation of this offering and the increased responsibilities of our directors as directors of a public company, our board of directors has adopted a non-employee director compensation policy, effective as of the effectiveness of the registration statement of which this prospectus forms a part, pursuant to which each of our directors who is not an employee or consultant of our company will be eligible to receive compensation for service on our board of directors and committees of our board of directors.

Each eligible director will receive an annual cash retainer of $40,000 for serving on our board of directors. The chairperson of the audit committee of our board of directors will be entitled an additional annual cash retainer of $15,000, and the chairpersons of each of the compensation and nominating and corporate governance committees of our board of directors will be entitled an additional annual cash retainer of $10,000. The members of the audit committee, who are not the chairperson of the committee, will be entitled to an additional annual cash retainer of $7,500, and the members of each of the compensation and nominating and corporate governance committees of our board of directors, who are not the chairpersons of such committees, will be entitled an additional annual cash retainer of $5,000.

In addition, on the date the registration statement of which this prospectus forms a part becomes effective, each eligible director, and each new eligible director who joins our board of directors after the pricing of this offering, will be granted a non-statutory stock option with a Black-Scholes value of $170,000 under our 2018 Plan, with the shares vesting in 36 equal monthly installments, subject to continued service as a director through the vesting date.

On the date of each annual meeting of our stockholders, each eligible director who continues to serve as a director of our company following the meeting will be granted a non-statutory stock option with a Black-Scholes value of $170,000 under our 2018 Plan, with the shares vesting on the earlier of the first anniversary of the date of grant or the next annual stockholders meeting, subject to continued service as a director though the applicable vesting date.

Each option awarded to eligible directors under the non-employee director compensation policy will be subject to accelerated vesting upon a Change in Control (as defined in the 2018 Plan).

The exercise price per share of each stock option granted under the non-employee director compensation policy will be equal to the closing price of our common stock on the Nasdaq Global Market on the date of grant. Each stock option will have a term of ten years from the date of grant, subject to earlier termination in connection with a termination of the eligible director's continuous service with us (provided that upon a termination of service other than for death, disability or cause, the post-termination exercise period will be 12 months from the date of termination).

## EXECUTIVE COMPENSATION

This section provides a summary of the compensation of our "named executive officers," who are the three executive officers listed in the "Summary Compensation Table" below. In addition to presenting quantitative compensation information in the tables below, this section also provides a qualitative description of the material factors helpful to an understanding of such data.

### Summary Compensation Table

The following table sets forth information regarding compensation awarded to, earned by and paid to our named executive officers with respect to the year ended December 31, 2017.

| Name and Principal Position | Salary ($) | Option Awards ($)[1] | Non-Equity Incentive Plan Compensation ($)[2] | All Other Compensation ($) | Total ($) |
|---|---|---|---|---|---|
| Jonathan P. Mow[3]<br>*Chief Executive Officer* | 338,250 | 22,375 | 74,778 | 794 | 436,197 |
| John Sharp<br>*Chief Financial Officer* | 307,500 | 8,950 | 50,985 | 711 | 368,146 |
| John Lee, M.D., Ph.D.<br>*Chief Medical Officer* | 307,500 | 11,188 | 50,985 | 711 | 370,384 |

(1) This column reflects the aggregate grant date fair value of option awards granted during the year measured pursuant to Financial Accounting Standard Board Accounting Standards Codification Topic 718, the basis for computing stock-based compensation in our financial statements. This calculation assumes that the named executive officer will perform the requisite service for the award to vest in full as required by SEC rules. The assumptions we used in valuing options are described in note 10 to our financial statements included in this prospectus. These amounts do not reflect the actual economic value that will be realized by the named executive officer upon vesting of the stock options, the exercise of the stock options, or the sale of the common stock underlying such stock options.

(2) See "—Narrative to Summary Compensation Table—Non-Equity Incentive Plan Compensation" below for a description of the material terms of the program pursuant to which this compensation was awarded.

(3) Mr. Mow is also a member of our board of directors, but did not receive any additional compensation in his capacity as a director.

### Narrative to Summary Compensation Table

The compensation committee of our board of directors has historically determined our executives' compensation and determines the compensation of our named executive officers. Our compensation committee typically reviews and discusses management's proposed compensation with the Chief Executive Officer for all executives other than the Chief Executive Officer. Based on those discussions and its discretion, the compensation committee then approves the compensation of each executive officer after discussions without members of management present.

#### *Annual Base Salary*

The annual base salaries of our named executive officers are generally determined, approved and reviewed periodically by our compensation committee in order to compensate our named executive officers for the satisfactory performance of duties to our company. Annual base salaries are intended to provide a fixed component of compensation to our named executive officers, reflecting their skill sets, experience, roles and responsibilities. Base salaries for our named executive officers have generally been set at levels deemed necessary to attract and retain individuals with superior talent.

The following table sets forth the annual base salaries for each of our named executive officers for 2017 and 2018, as determined by the compensation committee:

| Name | 2017 Base Salary ($) | 2018 Base Salary ($) |
|---|---|---|
| Jonathan P. Mow | 339,900 | 350,097 |
| John Sharp | 309,000 | 318,270 |
| John Lee | 309,000 | 318,270 |

Effective upon consummation of this offering, the base salaries of our named executive officers will be $402,600 for Mr. Mow, $329,700 for Mr. Sharp and $366,000 for Dr. Lee.

***Non-Equity Incentive Plan Compensation***

The compensation committee develops a performance-based bonus program annually. Under the 2017 annual performance bonus program, each named executive officer was eligible to be considered for an annual performance bonus based on (1) the individual's target bonus, as a percentage of base salary and (2) the percentage attainment of our 2017 corporate goals established by the compensation committee in its sole discretion and communicated to each officer. For 2017, Mr. Mow's target bonus percentage was 40% and each of Mr. Sharp's and Dr. Lee's target bonus percentage was 30%. The compensation committee determined that the percentage attainment of our corporate goals for 2017 was 55% and as a result, each of our named executive officers earned a 2017 performance bonus equal to 55% of his target bonus, as reflected in the column of the Summary Compensation Table above entitled "Non-Equity Incentive Plan Compensation." Effective upon consummation of this offering, the target bonus percentages of our named executive officers will be 50% for Mr. Mow, 40% for Mr. Sharp and 40% for Dr. Lee.

***Equity-Based Awards***

Our equity-based incentive awards granted to our named executive officers are designed to align the interests of our named executive officers with those of our stockholders. Vesting of equity awards is generally tied to each officer's continuous service with us and serves as an additional retention measure. Our executives generally are awarded an initial new hire grant upon commencement of employment. Additional grants may occur periodically in order to specifically incentivize executives with respect to achieving certain corporate goals or to reward executives for exceptional performance.

In April 2017, the compensation committee granted options to purchase 22,597 shares to Mr. Mow, 9,038 shares to Mr. Sharp and 13,558 shares to Dr. Lee, each at an exercise price of $1.428 per share. For each named executive officer, the shares subject to the award vest in equal monthly installments over 48 months from the date of grant.

In May 2018, the compensation committee granted options to purchase 22,597 shares to Mr. Mow, 9,038 shares to Mr. Sharp and 18,077 shares to Dr. Lee, each at an exercise price of $2.257 per share. For each named executive officer, the shares subject to the award vest in equal monthly installments over 48 months from the date of grant.

In October 2018, the compensation committee and board of directors approved an option to purchase 220,000 shares to Mr. Mow, which will be granted effective as of the execution and delivery of the underwriting agreement relating to this offering and will have a per share exercise price equal to the initial public offering price. The option vests in equal monthly installments over 48 months from the date of grant.

## Outstanding Equity Awards as of December 31, 2017

The following table sets forth certain information about outstanding equity awards granted to our named executive officers that remain outstanding as of December 31, 2017.

| | Option Awards[1] | | | | |
|---|---|---|---|---|---|
| Name | Grant Date | Number of Securities Underlying Unexercised Options (#) Exercisable | Number of Securities Underlying Unexercised Options (#) Unexercisable | Option Exercise Price ($)[2] | Option Expiration Date |
| Jonathan P. Mow | 12/18/2012 | 19,913 | — | 2.268 | 12/18/2022 |
| | 12/18/2012 | — | 32,553[3] | 2.268 | 12/18/2022 |
| | 3/31/2014 | 17,935 | 1,196[4] | 1.240 | 3/31/2024 |
| | 11/4/2014 | 140,732 | 37,035[4] | 1.240 | 11/4/2024 |
| | 5/12/2016 | 55,748 | 71,676[4] | 1.682 | 5/12/2026 |
| | 4/21/2017 | 4,237 | 18,360[4] | 1.428 | 4/21/2027 |
| John Sharp | 5/12/2016 | 56,493 | 79,089[5] | 1.682 | 5/12/2026 |
| | 4/21/2017 | 1,695 | 7,343[4] | 1.428 | 4/21/2027 |
| John Lee | 5/12/2016 | 56,493 | 79,089[5] | 1.682 | 5/12/2026 |
| | 4/21/2017 | 2,542 | 11,016[4] | 1.428 | 4/21/2027 |

(1) All of the awards listed in this table were granted under our Amended and Restated 2002 Stock Plan, the terms of which are described below under "—Equity Incentive Plans—Amended and Restated 2002 Stock Plan."

(2) All of the option awards listed in the table were granted with a per share exercise price equal to or above the estimated fair value of our common stock on the date of grant, as determined in good faith by our board of directors.

(3) The shares subject to this award vest in full upon a liquidation event with a net present value of at least $200 million, subject to the executive officer's continued service as of such liquidation event. For this purpose, a liquidation event is defined as any liquidation, dissolution or winding up of us, including by acquisition of us by another entity (unless our stockholders hold at least 50% of the voting power of the surviving or acquiring entity).

(4) The shares subject to this award vest in equal monthly installments over 48 months from the date of grant subject to the executive officer's continued service.

(5) 25% of the shares subject to this award vested on April 11, 2017, with the remainder of the shares vesting in equal monthly installments over 36 months subject to the executive officer's continued service.

On and after this offering, we may, on an annual basis or otherwise, grant additional equity awards to our executive officers pursuant to our 2018 Equity Incentive Plan, or the 2018 Plan, the terms of which are described below under "—Equity Incentive Plans—2018 Equity Incentive Plan."

## Retirement Benefits and Other Compensation

Our named executive officers did not participate in, or otherwise receive any benefits under, any pension, retirement or deferred compensation plan sponsored by us during 2017 other than our 401(k) plan described below. Our named executive officers were eligible to participate in our employee benefits, including health insurance and group life insurance benefits, on the same basis as our other employees. We maintain a 401(k) plan intended to qualify as a tax-qualified plan under Section 401 of the U.S. Internal Revenue Code of 1986, as amended, or the Code, which our named executive officers are eligible to participate in on the same basis as our other employees. We generally do not provide perquisites or personal benefits except in limited circumstances, and we did not provide any perquisites or personal benefits to our named executive officers in 2017.

## Agreements with our Named Executive Officers

In connection with his commencement of employment with us as our Chief Business Officer, we entered into an offer letter agreement with Mr. Mow in November 2012, which was amended in March 2014. Mr. Mow's

employment under the offer letter is at will and may be terminated at any time by us or by him. The offer letter provides for an initial base salary, bonus opportunity and equity award grants to Mr. Mow in his previous capacity as Chief Business Officer. In addition, the offer letter provides for a severance payment of six month's base salary upon Mr. Mow's termination without cause or upon his termination or resignation under certain circumstances within one year following a liquidation event (defined as any liquidation, dissolution or winding up of us, including by acquisition of us by another entity (unless our stockholders hold at least 50% of the voting power of the surviving or acquiring entity) or the sale, lease or other disposition of all or substantially all of our assets). Mr. Mow's compensation has been subsequently increased to the amounts described above and Mr. Mow was promoted to Chief Executive Officer in September 2014.

We also entered into offer letter agreements with each of Mr. Sharp and Dr. Lee in March 2016 in connection with each of their commencement of employment with us. Each offer letter is at will and may be terminated at any time by us or the executive officer. Each offer letter provides for an initial base salary, bonus opportunity and equity award grants, as well as participation in the change of control severance benefit plan described below under "—Potential Payments Upon Termination or Change in Control." Each of Mr. Sharp's and Dr. Lee's compensation has been subsequently increased to the amounts described above. We do not maintain any other offer letters or employment agreements with our named executive officers.

**Potential Payments Upon Termination or Change in Control**

We maintain a change of control severance benefit plan, or the Pre-IPO Severance Plan, and have entered into a severance benefit plan participation agreement under such plan with each of our named executive officers. Pursuant to these agreements, upon an "involuntary termination" (as defined below) in connection with or within a 12-month period following a "change in control" (as defined below), subject to execution of a release of claims against the company, each of our named executive officers will be entitled to a lump sum payment equal to 12 months of base salary and a prorated bonus, accelerated vesting of all outstanding equity awards and payment of 12 months of medical, dental and vision premiums. In addition, the post-termination exercise period applicable to all outstanding equity awards will be extended until the one year anniversary of termination. Any payments due to Mr. Mow under the Pre-IPO Severance Plan would be reduced by any severance payments due to him under his offer letter, to avoid duplication of benefits.

For purposes of the Pre-IPO Severance Plan, the following definitions apply:

- "involuntary termination" generally means a termination by us other than for death, disability or "cause" (as defined below) or a termination for "good reason" (as defined below).

- "cause" generally means the occurrence of any of the following events, conditions or actions with respect to the executive: (1) refusal or failure to perform the executive's material, lawful and appropriate duties; (2) material violation of our company's policy or any written agreement between our company and the executive; (3) repeated unexplained or unjustified absence from our company; (4) intentional or negligent misconduct; (5) conviction of, or the entering of a plea of *nolo contendere* with respect to, any felony or a crime involving moral turpitude; (6) unauthorized use or disclosure of proprietary information or trade secrets; (7) commitment of any act of fraud, embezzlement, misappropriation, dishonesty or breach of fiduciary duty against our company that causes, or is likely to cause, material harm to our company or is intended to result in substantial personal enrichment; or (8) failure to cooperate with our company in any investigation or formal proceeding.

- "good reason" generally means the following events, conditions or actions taken by our company without the executive's written consent: (1) a material reduction or material adverse change in job duties, responsibilities or authority inconsistent with the executive's position; (2) a material reduction of the executive's annual base salary, which is a reduction of at least 10% of such executive's base salary (unless pursuant to a salary reduction applicable generally to executive officers); (3) a material reduction in the executive's target bonus opportunity (unless pursuant to a base salary reduction generally applicable to executive officers); (4) a relocation of the executive's principal place of

employment that is more than 50 miles from executive's then-current principal place of employment; (5) a material breach of the change in control severance benefit plan or any other written agreement between the executive and our company; or (6) the failure of a buyer to assume the obligations of the change in control severance benefit plan.

- "change in control" generally means the following events: (1) any sale or exchange of our company's capital stock in one transaction or a series of transactions where more than 50% of our company's voting power is acquired by a person or entity or group of related entities; (2) reorganization, consolidation or merger where the outstanding voting securities of our company immediately before the transaction represent or are converted into less than 50% of our company's voting power immediately after the transaction; (3) consummation of a transaction or series of transactions that results in the sale of all or substantially all of our company's assets; or (4) any "person" or "group" (as defined in the Exchange Act) becoming the "beneficial owners" (as defined in Rule 13d-3 under the Exchange Act), directly or indirectly, of securities representing more than 50% of the voting power of our company then outstanding.

In addition to the Pre-IPO Severance Plan, Mr. Mow is entitled to severance pay under the terms of his offer letter agreement upon certain types of terminations as described above under "—Agreements with our Named Executive Officers" and each of our named executive officers holds equity awards granted subject to the general terms of our Amended and Restated 2002 Stock Plan, or the 2002 Plan. A description of the termination and change in control provisions of the 2002 Plan and the applicable awards granted to such officer is provided below under "—Equity Incentive Plans" and above under "—Narrative to Summary Compensation Table—Equity-Based Awards" and "—Outstanding Equity Awards as of December 31, 2017."

Effective upon consummation of this offering, each of our named executive officers will be eligible to receive severance benefits under the terms of our severance benefit plan adopted by the board of directors in October 2018 prior to this offering, or the Post-IPO Severance Plan, which will become effective in connection with this offering. The Post-IPO Severance Plan provides for severance benefits to the named executive officers upon (i) a "change in control termination" (as defined below) or (ii) a "regular termination" (defined below). Upon a change in control termination, each of our named executive officers is entitled to a lump sum payment equal to a portion of his base salary (18 months for Mr. Mow and 12 months for each of Mr. Sharp and Dr. Lee), payment of his target bonus, accelerated vesting of all outstanding equity awards, payment of COBRA premiums for a period of time (up to 18 months for Mr. Mow and 12 months for each of Mr. Sharp and Dr. Lee) and an extension of the post-termination exercise period applicable to his outstanding equity awards for up to one year following such termination. Upon a regular termination, each of our named executive officers is entitled to a lump sum payment equal to a portion of his base salary (12 months for Mr. Mow and 9 months for each of Mr. Sharp and Dr. Lee) and payment of COBRA premiums for a period of time (up to 12 months for Mr. Mow and 9 months for each of Mr. Sharp and Dr. Lee). All severance benefits under the Post-IPO Severance Plan are subject to the executive's execution of an effective release of claims against the company. The benefits under the Post-IPO Severance Plan will supersede the severance benefits under the Pre-IPO Severance Plan and under Mr. Mow's offer letter.

For purposes of the Post-IPO Severance Plan, the following definitions apply:

- "change in control termination" is an "involuntary termination" that occurs one month before or twelve months following a change in control (as defined in the 2018 Equity Incentive Plan);

- "regular termination" is an "involuntary termination" that does not occur within the one month before or twelve months following a change in control; and

- "involuntary termination" generally has the same meaning as in the Pre-IPO Severance Plan, except that "cause" for purposes of such definition has the meaning set forth in the 2018 Equity Incentive Plan.

**Equity Incentive Plans**

***2018 Equity Incentive Plan***

Our board of directors adopted our 2018 Equity Incentive Plan, or the 2018 Plan, in October 2018 and our stockholders approved our 2018 Plan in October 2018. Our 2018 Plan is a successor to and continuation of our Amended and Restated 2002 Stock Plan, or the 2002 Plan (described below). No stock awards may be granted under the 2018 Plan until the date of the underwriting agreement related to this offering. Once the 2018 Plan is effective, no further grants will be made under the 2002 Plan.

*Stock Awards.* Our 2018 Plan provides for the grant of incentive stock options, or ISOs, within the meaning of Section 422 of the Code, to employees, including employees of any parent or subsidiary, and for the grant of nonstatutory stock options, or NSOs, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance stock awards, performance cash awards and other forms of stock awards to employees, directors and consultants, including employees and consultants of our affiliates.

*Authorized Shares.* Initially, the maximum number of shares of our common stock that may be issued under our 2018 Plan after it becomes effective will be 3,231,626 shares, which is the sum of (1) 1,878,041 new shares, plus (2) the number of shares (not to exceed 1,353,585 shares) (A) that remain available for the issuance of awards under our 2002 Plan at the time our 2018 Plan becomes effective, and (B) any shares subject to outstanding stock options or other stock awards that were granted under our 2002 Plan that terminate or expire prior to exercise or settlement; are forfeited because of the failure to vest; or are reacquired or withheld (or not issued) to satisfy a tax withholding obligation or the purchase or exercise price. In addition, the number of shares of our common stock reserved for issuance under our 2018 Plan will automatically increase on January 1 of each calendar year, starting on January 1, 2019 (assuming the 2018 Plan becomes effective in 2018) through January 1, 2028, in an amount equal to 3% of the total number of shares of our capital stock outstanding on the last day of the calendar month before the date of each automatic increase, or a lesser number of shares determined by our board of directors. The maximum number of shares of our common stock that may be issued on the exercise of ISOs under our 2018 Plan is 9,694,878.

Shares subject to stock awards granted under our 2018 Plan that expire or terminate without being exercised in full or that are paid out in cash rather than in shares do not reduce the number of shares available for issuance under our 2018 Plan. If any shares of common stock issued pursuant to a stock award are forfeited back to or repurchased or reacquired by us for any reason, the shares that are forfeited or repurchased or reacquired will revert to and again become available for issuance under the 2018 Plan. Any shares reacquired in satisfaction of tax withholding obligations or as consideration for the exercise or purchase price of a stock award will again become available for issuance under the 2018 Plan.

The maximum number of shares of common stock subject to stock awards granted under the 2018 Plan or otherwise during a single calendar year to any non-employee director, taken together with any cash fees paid by us to such non-employee director during such calendar year for service on the board of directors, will not exceed $750,000 in total value (calculating the value of any such stock awards based on the grant date fair value of such stock awards for financial reporting purposes), or, with respect to the calendar year in which a non-employee director is first appointed or elected to the board of directors, $1,000,000.

*Plan Administration.* Our board of directors, or a duly authorized committee of our board of directors, will administer our 2018 Plan and is referred to as the "plan administrator" herein. Our board of directors may also delegate to one or more of our officers the authority to (1) designate employees (other than officers) to receive specified stock awards and (2) determine the number of shares subject to such stock awards. Under our 2018 Plan, our board of directors has the authority to determine award recipients, grant dates, the numbers and types of stock awards to be granted, the applicable fair market value, and the provisions of each stock award, including the period of exercisability and the vesting schedule applicable to a stock award.

Under the 2018 Plan, the board of directors also generally has the authority to effect, with the consent of any adversely affected participant, (1) the reduction of the exercise, purchase, or strike price of any outstanding

award; (2) the cancellation of any outstanding award and the grant in substitution therefore of other awards, cash, or other consideration; or (3) any other action that is treated as a repricing under generally accepted accounting principles.

*Stock Options.* ISOs and NSOs are granted under stock option agreements adopted by the plan administrator. The plan administrator determines the exercise price for stock options, within the terms and conditions of the 2018 Plan, provided that the exercise price of a stock option generally cannot be less than 100% of the fair market value of our common stock on the date of grant. Options granted under the 2018 Plan vest at the rate specified in the stock option agreement as determined by the plan administrator.

The plan administrator determines the term of stock options granted under the 2018 Plan, up to a maximum of 10 years. Unless the terms of an optionholder's stock option agreement provide otherwise, if an optionholder's service relationship with us or any of our affiliates ceases for any reason other than disability, death, or cause, the optionholder may generally exercise any vested options for a period of three months following the cessation of service. This period may be extended in the event that exercise of the option is prohibited by applicable securities laws or our insider trading policy. If an optionholder's service relationship with us or any of our affiliates ceases due to death, or an optionholder dies within a certain period following cessation of service, the optionholder or a beneficiary may generally exercise any vested options for a period of 18 months following the date of death. If an optionholder's service relationship with us or any of our affiliates ceases due to disability, the optionholder may generally exercise any vested options for a period of 12 months following the cessation of service. In the event of a termination for cause, options generally terminate upon the termination date. In no event may an option be exercised beyond the expiration of its term.

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

Unless the plan administrator provides otherwise, options generally are not transferable except by will or the laws of descent and distribution. Subject to approval of the plan administrator or a duly authorized officer in each case, (1) an option may be transferred pursuant to a domestic relations order, official marital settlement agreement or other divorce or separation instrument and (2) an optionholder may designate a beneficiary who may exercise the option following the optionholder's death.

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

*Restricted Stock Unit Awards.* Restricted stock unit awards are granted under restricted stock unit award agreements adopted by the plan administrator. Restricted stock unit awards may be granted in consideration for any form of legal consideration that may be acceptable to our board of directors and permissible under applicable law. A restricted stock unit award may be settled by cash, delivery of stock, a combination of cash and stock as deemed appropriate by the plan administrator or in any other form of consideration set forth in the restricted stock unit award agreement. Additionally, dividend equivalents may be credited in respect of shares covered by a restricted stock unit award. Except as otherwise provided in the applicable award agreement, restricted stock unit awards that have not vested will be forfeited once the participant's continuous service ends for any reason.

*Restricted Stock Awards.* Restricted stock awards are granted under restricted stock award agreements adopted by the plan administrator. A restricted stock award may be awarded in consideration for cash, check,

bank draft or money order, past or future services to us or any other form of legal consideration that may be acceptable to our board of directors and permissible under applicable law. The plan administrator determines the terms and conditions of restricted stock awards, including vesting and forfeiture terms. If a participant's service relationship with us ends for any reason, we may receive any or all of the shares of common stock held by the participant that have not vested as of the date the participant terminates service with us through a forfeiture condition or a repurchase right.

*Stock Appreciation Rights.* Stock appreciation rights are granted under stock appreciation right agreements adopted by the plan administrator. The plan administrator determines the purchase price or strike price for a stock appreciation right, which generally cannot be less than 100% of the fair market value of our common stock on the date of grant. A stock appreciation right granted under the 2018 Plan vests at the rate specified in the stock appreciation right agreement as determined by the plan administrator.

The plan administrator determines the term of stock appreciation rights granted under the 2018 Plan, up to a maximum of 10 years. If a participant's service relationship with us or any of our affiliates ceases for any reason other than cause, disability, or death, the participant may generally exercise any vested stock appreciation right for a period of three months following the cessation of service. This period may be further extended in the event that exercise of the stock appreciation right following such a termination of service is prohibited by applicable securities laws or our insider trading policy. If a participant's service relationship with us, or any of our affiliates, ceases due to disability or death, or a participant dies within a certain period following cessation of service, the participant or a beneficiary may generally exercise any vested stock appreciation right for a period of 12 months in the event of disability and 18 months in the event of death. In the event of a termination for cause, stock appreciation rights generally terminate immediately upon the occurrence of the event giving rise to the termination of the individual for cause. In no event may a stock appreciation right be exercised beyond the expiration of its term.

*Performance Awards.* The 2018 Plan permits the grant of performance-based stock and cash awards. Our compensation committee may structure awards so that the stock or cash will be issued or paid only following the achievement of certain pre-established performance goals during a designated performance period.

The performance goals that may be selected include one or more of the following: (1) sales; (2) revenues; (3) assets; (4) expenses; (5) market penetration or expansion; (6) earnings from operations; (7) earnings before or after deduction for all or any portion of interest, taxes, depreciation, amortization, incentives, service fees or extraordinary or special items, whether or not on a continuing operations or an aggregate or per share basis; (8) net income or net income per common share (basic or diluted); (9) return on equity, investment, capital or assets; (10) one or more operating ratios; (11) borrowing levels, leverage ratios or credit rating; (12) market share; (13) capital expenditures; (14) cash flow, free cash flow, cash flow return on investment or net cash provided by operations; (15) stock price, dividends or total stockholder return; (16) development of new technologies or products; (17) sales of particular products or services; (18) economic value created or added; (19) operating margin or profit margin; (20) customer acquisition or retention; (21) raising or refinancing of capital; (22) successful hiring of key individuals; (23) resolution of significant litigation; (24) acquisitions and divestitures (in whole or in part); (25) joint ventures and strategic alliances; (26) spin-offs, split-ups and the like; (27) reorganizations; (28) recapitalizations, restructurings, financings (issuance of debt or equity) or refinancings; (29) or strategic business criteria, consisting of one or more objectives based on the following goals: achievement of timely development, design management or enrollment, meeting specified market penetration or value added, payor acceptance, patient adherence, peer reviewed publications, issuance of new patents, establishment of or securing of licenses to intellectual property, product development or introduction (including, without limitation, any clinical trial accomplishments, regulatory or other filings, approvals or milestones, discovery of novel products, maintenance of multiple products in pipeline, product launch or other product development milestones), geographic business expansion, cost targets, cost reductions or savings, customer satisfaction, operating efficiency, acquisition or retention, employee satisfaction, information technology, corporate development (including, without limitation, licenses, innovation, research or establishment of third party collaborations), manufacturing or process development, legal compliance or risk reduction, patent application or

issuance goals, or goals relating to acquisitions, divestitures or other business combinations (in whole or in part), joint ventures or strategic alliances; and (30) other measures of performance selected by the board of directors.

The performance goals may be based on Company-wide performance or performance of one or more business units, divisions, affiliates or business segments, and may be either absolute or relative to the performance of one or more comparable companies or the performance of one or more relevant indices. Our board of directors is authorized at any time in its sole discretion, to adjust or modify the calculation of a performance goal for such performance period in order to prevent the dilution or enlargement of the rights of participants, (1) in the event of, or in anticipation of, any unusual or extraordinary corporate item, transaction, event or development; (2) in recognition of, or in anticipation of, any other unusual or nonrecurring events affecting us, or our financial statements in response to, or in anticipation of, changes in applicable laws, regulations, accounting principles, or business conditions; or (3) in view of the board of director's assessment of our business strategy of, performance of comparable organizations, economic and business conditions, and any other circumstances deemed relevant. Specifically, the board of directors is authorized to make adjustment in the method of calculating attainment of performance goals and objectives for a performance period as follows: (A) to exclude the dilutive effects of acquisitions or joint ventures; (B) to assume that any business divested by us achieved performance objectives at targeted levels during the balance of a performance period following such divestiture; and (C) to exclude the effect of any change in the outstanding shares of our common stock by reason of any stock dividend or split, stock repurchase, reorganization, recapitalization, merger, consolidation, spin-off, combination or exchange of shares or other similar corporate change, or any distributions to common stockholders other than regular cash dividends. In addition, the board of directors is authorized to make adjustment in the method of calculating attainment of performance goals and objectives for a performance period as follows: (1) to exclude restructuring and/or other nonrecurring charges; (2) to exclude exchange rate effects, as applicable, for non-U.S. dollar denominated net sales and operating earnings; (3) to exclude the effects of changes to generally accepted accounting standards required by the Financial Accounting Standards Board; (4) to exclude the effects of any items that are "unusual" in nature or occur "infrequently" as determined under generally accepted accounting principles; (5) to exclude the effects to any statutory adjustments to corporate tax rates; and (6) to make other appropriate adjustments selected by the board of directors.

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

*Changes to Capital Structure*. In the event there is a specified type of change in our capital structure, such as a stock split, reverse stock split, or recapitalization, appropriate adjustments will be made to (1) the class and maximum number of shares reserved for issuance under the 2018 Plan, (2) the class and maximum number of shares by which the share reserve may increase automatically each year, (3) the class and maximum number of shares that may be issued on the exercise of ISOs, and (4) the class and number of shares and exercise price, strike price, or purchase price, if applicable, of all outstanding stock awards.

*Corporate Transactions*. Our 2018 Plan provides that in the event of certain specified significant corporate transactions (or a change in control, as defined below), unless otherwise provided in an award agreement or other written agreement between us and the award holder, the plan administrator may take one or more of the following actions with respect to such stock awards:

- arrange for the assumption, continuation or substitution of a stock award by a successor corporation;
- arrange for the assignment of any reacquisition or repurchase rights held by us to a successor corporation;
- accelerate the vesting, in whole or in part, of the stock award and provide for its termination if not exercised (if applicable) at or before the effective time of the transaction;

- arrange for the lapse, in whole or in part, of any reacquisition or repurchase rights held by us;
- cancel or arrange for the cancellation of the stock award, to the extent not vested or not exercised before the effective time of the transaction, in exchange for a cash payment, if any; or
- make a payment equal to the excess, if any, of (A) the value of the property the participant would have received on exercise of the award immediately before the effective time of the transaction, over (B) any exercise price payable by the participant in connection with the exercise.

The plan administrator is not obligated to treat all stock awards or portions of stock awards in the same manner and is not obligated to take the same actions with respect to all participants.

Under the 2018 Plan, a corporate transaction is generally the consummation of: (1) a sale of all or substantially all of our assets, (2) the sale or disposition of more than 50% of our outstanding securities, (3) a merger or consolidation where we do not survive the transaction or (4) a merger or consolidation where we do survive the transaction but the shares of our common stock outstanding immediately before such transaction are converted or exchanged into other property by virtue of the transaction.

*Change in Control.* In the event of a change in control, the plan administrator may take any of the above-mentioned actions. Awards granted under the 2018 Plan may be subject to additional acceleration of vesting and exercisability upon or after a change in control as may be provided in the applicable stock award agreement or in any other written agreement between the Company or any affiliate and the participant, including under the Post-IPO Severance Plan, but in the absence of such provision, no such acceleration will automatically occur. Under the 2018 Plan, a change in control is generally (1) the acquisition by any person or company of more than 50% of the combined voting power of our then outstanding stock, (2) a merger, consolidation or similar transaction in which our stockholders immediately before the transaction do not own, directly or indirectly, more than 50% of the combined voting power of the surviving entity (or the parent of the surviving entity) in substantially the same proportions as their ownership immediately prior to such transaction, (3) a sale, lease, exclusive license or other disposition of all or substantially all of our assets other than to an entity more than 50% of the combined voting power of which is owned by our stockholders in substantially the same proportions as their ownership of the outstanding voting securities of the Company immediately prior to such transaction, (4) a complete dissolution or liquidation of the Company or (5) when a majority of our board of directors becomes comprised of individuals who were not serving on our board of directors on the date of the underwriting agreement related to this offering, or the incumbent board, or whose nomination, appointment or election was not approved by a majority of the incumbent board still in office.

*Plan Amendment or Termination*. Our board of directors has the authority to amend, suspend or terminate our 2018 Plan, provided that such action does not materially impair the existing rights of any participant without such participant's written consent. Certain material amendments also require the approval of our stockholders. No ISOs may be granted after the tenth anniversary of the date our board of directors adopts our 2018 Plan. No stock awards may be granted under our 2018 Plan while it is suspended or after it is terminated.

***Amended and Restated 2002 Stock Plan***

Our board of directors and our stockholders approved our 2002 Plan on July 1, 2002. It was subsequently amended and restated in October 2012 and most recently amended by our board of directors in July 2018 and stockholders in August 2018. All references in this prospectus to the 2002 Plan shall be deemed to refer to our Amended and Restated 2002 Stock Plan, as amended, unless the context otherwise requires. As of June 30, 2018, there were 90,256 shares remaining available for the future grant of stock awards under our 2002 Plan. As of June 30, 2018, there were outstanding stock options covering a total of 1,210,776 shares of our common stock that were granted under our 2002 Plan.

*Stock Awards.* Our 2002 Plan provides for the grant of ISOs within the meaning of Section 422 of the Code to employees, including employees of any parent or subsidiary, and for the grant of NSOs, stock purchases and restricted stock awards to employees, directors and consultants, including employees and consultants of our affiliates. We have granted stock options and restricted stock awards, and permitted stock purchases, under the 2002 Plan.

*Authorized Shares.* Subject to certain capitalization adjustments, the aggregate number of shares of common stock that may be issued pursuant to stock awards under the 2002 Plan will not exceed 1,813,243 shares.

Shares subject to stock awards granted under our 2002 Plan that expire or terminate without being exercised in full do not reduce the number of shares available for issuance under our 2002 Plan. Additionally, if any shares issued pursuant to a stock award are forfeited back to or repurchased because of the failure to meet a contingency or condition required to vest, then the shares that are forfeited or repurchased will revert to and again become available for issuance under the 2002 Plan.

*Plan Administration.* Our board of directors, or a duly authorized committee of our board of directors, will administer our 2002 Plan and is referred to as the "plan administrator" herein. Under our 2002 Plan, the plan administrator has the authority to determine award recipients, dates of grant, the numbers and types of stock awards to be granted, the applicable fair market value and the provisions of each stock award, including the period of their exercisability, the vesting schedule applicable to a stock award and any repurchase rights that may apply.

Under the 2002 Plan, the plan administrator also generally has the authority to effect: (1) the reduction of the exercise, purchase, or strike price of any outstanding award; or (2) institute a program whereby outstanding ISOs or NSOs can be surrendered in exchange for ISOs or NSOs with a lower exercise price.

*Stock Options.* ISOs and NSOs are granted under stock option agreements adopted by the plan administrator. The plan administrator determines the exercise price for stock options, within the terms and conditions of the 2002 Plan, provided that the exercise price of a stock option generally cannot be less than 100% of the fair market value of our common stock on the date of grant. Options granted under the 2002 Plan vest at the rate specified in the stock option agreement as determined by the plan administrator.

The plan administrator determines the term of stock options granted under the 2002 Plan, up to a maximum of 10 years. If an optionholder's service relationship with us or any of our affiliates ceases for any reason other than disability, death or cause, the optionholder may generally exercise any vested options until the expiration of the option, unless otherwise provided for in the option agreement. If an optionholder's service relationship with us or any of our affiliates ceases due to death, or an optionholder dies within a certain period following cessation of service, the optionholder or a beneficiary may generally exercise any vested options for a period of 12 months following the date of death. If an optionholder's service relationship with us or any of our affiliates ceases due to disability, the optionholder may generally exercise any vested options for a period of 12 months following the cessation of service. In the event of a termination for cause, options generally terminate upon the termination date. In no event may an option be exercised beyond the expiration of its term.

Acceptable consideration for the purchase of common stock issued upon the exercise of a stock option will be determined by the plan administrator and may include: (1) cash or check, (2) a broker-assisted cashless exercise, (3) the tender of shares of our common stock previously owned by the optionholder, (4) a deferred payment arrangement, (5) the tender of shares issuable upon exercise of a stock right, or (6) other legal consideration approved by the plan administrator.

Unless the plan administrator provides otherwise, ISOs are not transferable except by will or the laws of descent and distribution. Awards other than ISOs generally are not transferable except: (1) to the grantee's family member, (2) by will or the laws of descent and distribution, or (3) pursuant to a qualified domestic relations order.

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

*Stock Purchase Awards.* Stock purchase awards are granted under stock purchase award agreements adopted by the plan administrator. The plan administrator determines the terms and conditions of stock purchase awards, including vesting and forfeiture terms. If a participant's service relationship with us ends for any reason, we may receive any or all of the shares of common stock held by the participant that have not vested as of the date the participant terminates service with us through a forfeiture condition or a repurchase right.

*Restricted Stock Awards.* Restricted stock awards are granted under restricted stock award agreements adopted by the plan administrator. The plan administrator determines the terms and conditions of restricted stock awards, including vesting and forfeiture terms. If a participant's service relationship with us ends for any reason, we may receive any or all of the shares of common stock held by the participant that have not vested as of the date the participant terminates service with us through a forfeiture condition or a repurchase right.

*Changes to Capital Structure*. In the event that our shares of common stock are subdivided or combined into a greater or smaller number of shares, or if we issue common stock as a stock dividend, then appropriate adjustments will be made to the number of shares of all outstanding stock awards.

*Corporate Transactions*. Our 2002 Plan provides that in the event of certain specified significant corporate transactions, unless otherwise provided by the plan administrator, the plan administrator shall take any action such that any outstanding awards under the 2002 Plan are either assumed or substituted with an equivalent award. Notwithstanding the foregoing, pursuant to the 2002 Plan, in the event that any surviving or acquiring corporation does not assume any or all outstanding awards or substitute similar stock awards, then, unless otherwise provided by the plan administrator, the vesting (and, if applicable, the exercisability) of such outstanding awards shall (contingent upon the effectiveness of the corporate transaction) be accelerated in full to a date prior to the effective time of the corporate transaction, and the outstanding awards shall terminate if not exercised (if applicable) at or prior to such effective time.

Under the 2002 Plan, a corporate transaction generally occurs if we are consolidated with or acquired by another entity in a merger or a sale of all or substantially all of our assets.

*Plan Amendment or Termination*. Our board of directors has the authority to amend, suspend, or terminate our 2002 Plan, provided that such action does not impair the existing rights of any participant without such participant's written consent. Certain material amendments also require the approval of our stockholders. Unless terminated sooner, the 2002 Plan will automatically terminate on October 12, 2022. No stock awards may be granted under our 2002 Plan while it is suspended or after it is terminated.

***2018 Employee Stock Purchase Plan***

Our board of directors adopted, and our stockholders approved, our 2018 Employee Stock Purchase Plan, or the ESPP, in October 2018. The ESPP will become effective immediately prior to and contingent upon the date of the underwriting agreement related to this offering. The purpose of the ESPP is to secure the services of new employees, to retain the services of existing employees and to provide incentives for such individuals to exert maximum efforts toward our success and that of our affiliates. The ESPP is intended to qualify as an "employee stock purchase plan" within the meaning of Section 423 of the Code for U.S. employees.

*Share Reserve*. Following this offering, the ESPP authorizes the issuance of 196,000 shares of our common stock under purchase rights granted to our employees or to employees of any of our designated affiliates. The

number of shares of our common stock reserved for issuance will automatically increase on January 1 of each calendar year, beginning on January 1, 2019 (assuming the ESPP becomes effective in 2018) through January 1, 2028, by the lesser of (1) 1% of the total number of shares of our common stock outstanding on the last day of the calendar month before the date of the automatic increase, and (2) 490,000 shares; provided that before the date of any such increase, our board of directors may determine that such increase will be less than the amount set forth in clauses (1) and (2). As of the date hereof, no shares of our common stock have been purchased under the ESPP.

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

*Payroll Deductions*. Generally, all regular employees, including executive officers, employed by us or by any of our designated affiliates, may participate in the ESPP and may contribute, normally through payroll deductions, up to 15% of their earnings (as defined in the ESPP) for the purchase of our common stock under the ESPP. Unless otherwise determined by our board of directors, common stock will be purchased for the accounts of employees participating in the ESPP at a price per share that is at least the lesser of (1) 85% of the fair market value of a share of our common stock on the first date of an offering or (2) 85% of the fair market value of a share of our common stock on the date of purchase.

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

*Changes to Capital Structure*. In the event that there occurs a change in our capital structure through such actions as a stock split, merger, consolidation, reorganization, recapitalization, reincorporation, stock dividend, dividend in property other than cash, large nonrecurring cash dividend, liquidating dividend, combination of shares, exchange of shares, change in corporate structure or similar transaction, the board of directors will make appropriate adjustments to: (1) the class(es) and maximum number of shares reserved under the ESPP, (2) the class(es) and maximum number of shares by which the share reserve may increase automatically each year, (3) the class(es) and number of shares subject to and purchase price applicable to outstanding offerings and purchase rights and (4) the class(es) and number of shares that are subject to purchase limits under ongoing offerings.

*Corporate Transactions*. In the event of certain significant corporate transactions, any then-outstanding rights to purchase our stock under the ESPP may be assumed, continued or substituted for by any surviving or acquiring entity (or its parent company). If the surviving or acquiring entity (or its parent company) elects not to assume, continue, or substitute for such purchase rights, then the participants' accumulated payroll contributions will be used to purchase shares of our common stock within 10 business days before such corporate transaction, and such purchase rights will terminate immediately.

Under the ESPP, a corporate transaction is generally the consummation of: (1) a sale of all or substantially all of our assets, (2) the sale or disposition of more than 50% of our outstanding securities, (3) a merger or

consolidation where we do not survive the transaction and (4) a merger or consolidation where we do survive the transaction but the shares of our common stock outstanding immediately before such transaction are converted or exchanged into other property by virtue of the transaction.

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

**Limitations on Liability and Indemnification Matters**

Upon the closing of this offering, our amended and restated certificate of incorporation will contain provisions that limit the liability of our current and former directors for monetary damages to the fullest extent permitted by Delaware law. Delaware law provides that directors of a corporation will not be personally liable for monetary damages for any breach of fiduciary duties as directors, except liability for:

- any breach of the director's duty of loyalty to the corporation or its stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law; or
- any transaction from which the director derived an improper personal benefit.

This limitation of liability does not apply to liabilities arising under federal securities laws and does not affect the availability of equitable remedies such as injunctive relief or rescission.

Our amended and restated bylaws to be in effect upon the closing of this offering will provide that we are required to indemnify our directors and executive officers to the fullest extent permitted by Delaware law. Our amended and restated bylaws will also provide that, upon satisfaction of certain conditions, we are required to advance expenses incurred by a director or executive officer in advance of the final disposition of any action or proceeding, and permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in that capacity regardless of whether we would otherwise be permitted to indemnify him or her under the provisions of Delaware law. Our amended and restated bylaws will also provide our board of directors with discretion to indemnify our other officers and employees when determined appropriate by our board of directors. We expect to enter into agreements to indemnify our directors, executive officers and other employees as determined by the board of directors. With certain exceptions, these agreements provide for indemnification for related expenses, including, among other things, attorneys' fees, judgments, fines and settlement amounts incurred by any of these individuals in any action or proceeding. We believe that these provisions and agreements are necessary to attract and retain qualified persons as directors and officers. We also maintain customary directors' and officers' liability insurance.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws to be in effect upon the closing of this offering may discourage stockholders from bringing a lawsuit against our directors for breach of their fiduciary duty. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and other stockholders. Further, a stockholder's investment may be adversely affected to the extent that we pay the costs of settlement and damage awards against directors and officers as required by these indemnification provisions. At present, there is no pending litigation or proceeding involving any of our directors, officers or employees for which indemnification is sought, and we are not aware of any threatened litigation that may result in claims for indemnification.

**Rule 10b5-1 Sales Plans**

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

**Emerging Growth Company Status**

As an emerging growth company we will be exempt from certain requirements related to executive compensation, including the requirements to hold a nonbinding advisory vote on executive compensation and to provide information relating to the ratio of total compensation of our Chief Executive Officer to the median of the annual total compensation of all of our employees, each as required by the Investor Protection and Securities Reform Act of 2010, part of the Dodd-Frank Wall Street Reform and Consumer Protection Act.

## CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

The following is a summary of transactions since January 1, 2015 to which we have been a participant in which the amount involved exceeded or will exceed $120,000, and in which any of our then directors, executive officers or holders of more than 5% of any class of our capital stock at the time of such transaction, or any members of their immediate family, had or will have a direct or indirect material interest, other than compensation arrangements which are described under the section titled "Executive Compensation."

### Participation in this Offering

Certain of our existing stockholders, including entities affiliated with certain of our directors and beneficial owners of greater than 5% of our capital stock, have indicated an interest in purchasing an aggregate of approximately $25.0 million in shares of our common stock in this offering at the initial public offering price per share. Based on an assumed initial public offering price of $13.00 per share, these persons and entities would purchase an aggregate of approximately 1,900,000 of the 5,000,000 shares in this offering based on these indications of interest. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any of these persons or entities, or any of these persons or entities may determine to purchase more, less or no shares in this offering.

### Our Relationship with AstraZeneca

In November 2017, we entered into an exclusive license agreement with MedImmune, a wholly owned subsidiary of AstraZeneca and an affiliate of Zeneca, Inc., a beneficial owner of more than 5% of our capital stock, or the MedImmune License. The MedImmune License is described more fully in "Business—Our License Agreements—MedImmune Limited." Under the MedImmune License, we paid MedImmune an upfront fee of $100,000 in November 2017. We are also required to pay MedImmune, among other things: 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. Our payments to MedImmune under the MedImmune License totaled $0.6 million in the aggregate during the year ended December 31, 2017.

### Private Placements of our Securities

#### *Series C Preferred Stock Financing*

In February 2015, we entered into a preferred stock purchase agreement, which was subsequently amended in July 2015, with certain investors, including beneficial owners of greater than 5% of our capital stock, pursuant to which we issued and sold to our related party investors an aggregate of 2,070,743 shares of Series C-1 redeemable convertible preferred stock, or the First Tranche Shares, at a purchase price of $9.659 per share for an aggregate purchase price of $20.0 million. We also agreed to issue and sell to our related party investors, upon our achievement of certain milestones, (1) up to an aggregate of 872,472 shares of Series C-2 redeemable convertible preferred stock at a purchase price of $11.462 per share and (2) up to an aggregate of 753,231 shares of Series C-3 redeemable convertible preferred stock at a purchase price of $13.28 per share. We discontinued development of the program related to these milestones and, therefore, we will not issue such milestone shares.

The following table sets forth the aggregate number of shares of Series C-1 redeemable convertible preferred stock issued to our related parties in this financing:

| Participants | Shares of Series C-1 Preferred Stock |
|---|---|
| Zeneca, Inc. | 1,553,060 |
| New Enterprise Associates 13, L.P.(1) | 260,865 |
| Entities affiliated with Hatteras Venture Partners(2) | 112,354 |
| Johnson & Johnson Innovation – JJDC, Inc. | 85,280 |
| Entities affiliated with Fletcher Spaght Ventures(3) | 59,184 |

(1) New Enterprise Associates 13, L.P., or NEA 13, is affiliated with Peter Justin Klein and Bibhash Mukhopadhyay, members of our board of directors.

(2) Affiliates of Hatteras Venture Partners whose securities are aggregated for purposes of reporting share ownership information are: Hatteras Venture Partners III, LP, or HVP III, and Hatteras Venture Affiliates III, LP, or HV Affiliates. Hatteras Venture Partners is affiliated with Clay B. Thorp, our chairman.

(3) Affiliates of Fletcher Spaght Ventures whose securities are aggregated for purposes of reporting share ownership information are: Fletcher Spaght Ventures II, LP, or Fletcher Spaght Ventures II, FSV II, LP or FSV II, and FSV II-B, LP, or FSV II-B. Fletcher Spaght Ventures is affiliated with Linda Tufts, a member of our board of directors.

In February 2015, we issued 25,883 shares of Series B redeemable convertible preferred stock to HVP III and HV Affiliates as a success fee in connection with the issuance and sale of the First Tranche Shares.

***Issuance of Series B Preferred Stock upon Conversion of Convertible Promissory Notes***

In February 2015, certain of our investors, including directors, executive officers and beneficial owners of greater than 5% of our capital stock, elected to convert their outstanding convertible promissory notes in the aggregate principal amount of $9.5 million into an aggregate of 1,106,160 shares of Series B redeemable convertible preferred stock.

The following table sets forth for each of our related parties the aggregate number of shares of Series B redeemable convertible preferred stock issued, and the corresponding aggregate principal amount of convertible promissory notes so converted, in this transaction:

| Participants | Principal Amount of Convertible Promissory Notes Converted ($) | Shares of Series B Preferred Stock Issued upon Conversion of Notes |
|---|---|---|
| New Enterprise Associates 13, L.P. (1) | 4,735,524 | 553,364 |
| Johnson & Johnson Innovation – JJDC, Inc. | 1,548,111 | 180,902 |
| Entities affiliated with Hatteras Venture Partners(2) | 2,008,235 | 234,668 |
| Entities affiliated with Fletcher Spaght Ventures(3) | 1,074,401 | 125,544 |
| Ashutosh Chilkoti, Ph.D.(4) | 40,000 | 4,673 |
| Entities affiliated with Jonathan P. Mow(5) | 30,000 | 3,505 |
| Peter Justin Klein, M.D., J.D. | 10,000 | 1,168 |
| Susan Arnold, Ph.D. | 10,000 | 1,168 |
| Joel Sussman(6) | 10,000 | 1,168 |

(1) NEA 13 is affiliated with Peter Justin Klein and Bibhash Mukhopadhyay, members of our board of directors.

(2) Affiliates of Hatteras Venture Partners whose securities are aggregated for purposes of reporting share ownership information are: HVP III and HV Affiliates. Hatteras Venture Partners is affiliated with Clay B. Thorp, our chairman.

(3) Affiliates of Fletcher Spaght Ventures whose securities are aggregated for purposes of reporting share ownership information are: Fletcher Spaght Ventures II, FSV II and FSV II-B. Fletcher Spaght Ventures is affiliated with Linda Tufts, a member of our board of directors.

(4) Ashutosh Chilkoti served as a member of our board of directors at the time of this transaction.

(5) Mow Trust dated April 17, 2008, of which Mr. Mow is the sole trustee.

(6) Joel Sussman served as our Chief Financial Officer at the time of this transaction.

***Convertible Promissory Notes and Series C-1 Warrant Financing***

In January 2017, we entered into a note and warrant purchase agreement with certain investors, including holders of greater than 5% of our capital stock, pursuant to which we (1) issued and sold to our related party investors convertible promissory notes in the aggregate principal amount of $6.5 million, which have an annual interest rate of 8%, (2) issued to our related party investors related warrants to purchase shares of Series C-1 redeemable convertible preferred stock at $0.12 per share and (3) reserved the option at any time on or after March 31, 2017 to sell to our related party investors additional convertible promissory notes on the same terms in the aggregate principal amount of up to $7.9 million. In October 2017, we exercised in full the option to sell such additional notes, which resulted in an increase in the number of shares of Series C-1 redeemable convertible preferred stock issuable pursuant to the warrants. The aggregate principal amount of convertible promissory notes outstanding and held by related parties as of June 30, 2018 was $14.4 million, and, to date, we have not paid any interest on the convertible promissory notes.

The following table sets forth the aggregate principal amount of convertible promissory notes and shares of Series C-1 redeemable convertible preferred stock issuable upon the exercise of warrants issued to our related parties in this financing:

| Participants | Principal Amount of Convertible Promissory Notes ($) | Shares of Series C-1 Preferred Stock Issuable Pursuant to Warrants |
|---|---|---|
| New Enterprise Associates 13, L.P. [1] | 5,750,000 | 119,067 |
| Zeneca, Inc. | 4,500,000 | 93,184 |
| Johnson & Johnson Innovation – JJDC, Inc. | 2,000,000 | 41,414 |
| Entities affiliated with Hatteras Venture Partners[2] | 1,500,000 | 31,061 |
| Entities affiliated with Fletcher Spaght Ventures[3] | 600,000 | 12,424 |

(1) NEA 13 is affiliated with Peter Justin Klein and Bibhash Mukhopadhyay, members of our board of directors.

(2) Affiliates of Hatteras Venture Partners whose securities are aggregated for purposes of reporting share ownership information are: HVP III, HV Affiliates and Venture Capital Multiplier Fund, or Multiplier Fund. Hatteras Venture Partners is affiliated with Clay B. Thorp, our chairman.

(3) Affiliates of Fletcher Spaght Ventures whose securities are aggregated for purposes of reporting share ownership information are: Fletcher Spaght Ventures II, FSV II and FSV II-B. Fletcher Spaght Ventures is affiliated with Linda Tufts, a member of our board of directors.

***Series D Preferred Stock Financing and Issuance of Series D Preferred Stock and Series C-1 Warrants Upon Conversion of Convertible Promissory Notes***

In August 2018, we entered into a preferred stock purchase agreement with certain investors, including beneficial owners of greater than 5% of our capital stock, pursuant to which we issued and sold to our related party investors an aggregate of 740,292 shares of Series D redeemable convertible preferred stock at a purchase price of $9.659 per share for an aggregate cash purchase price of $7.2 million and issued to such related party investors warrants to purchase 148,054 shares of Series C-1 redeemable convertible preferred stock. Certain of our investors, including beneficial owners of greater than 5% of our capital stock, elected to convert their outstanding convertible promissory notes in the aggregate principal amount of $14.4 million into an aggregate of 2,030,680 shares of Series D redeemable convertible preferred stock.

The following table sets forth for each of our related parties the aggregate number of shares of Series D redeemable convertible preferred stock and warrants to purchase Series C-1 redeemable convertible preferred stock issued, and the corresponding aggregate principal amount of convertible promissory notes so converted, in this transaction:

| Participants | Principal Amount of Convertible Promissory Notes Converted ($) | Shares of Series D Preferred Stock Sold and Issued Pursuant to Conversion of Convertible Promissory Notes | Warrants to Purchase Shares of Series C-1 Preferred Stock |
|---|---|---|---|
| New Enterprise Associates 13, L.P. (1) | 5,750,000 | 1,124,301 | 62,123 |
| Zeneca, Inc. | 4,500,000 | 740,337 | 20,707 |
| Johnson & Johnson Innovation – JJDC, Inc. | 2,000,000 | 283,022 | — |
| Entities affiliated with Hatteras Venture Partners (2) | 1,500,000 | 522,877 | 62,120 |
| Entities affiliated with Fletcher Spaght Ventures (3) | 600,000 | 100,435 | 3,104 |

(1) NEA 13 is affiliated with Peter Justin Klein and Bibhash Mukhopadhyay, members of our board of directors.

(2) Affiliates of Hatteras Venture Partners whose securities are aggregated for purposes of reporting share ownership information are: HVP III, HV Affiliates and Multiplier Fund. Hatteras Venture Partners is affiliated with Clay B. Thorp, our chairman.

(3) Affiliates of Fletcher Spaght Ventures whose securities are aggregated for purposes of reporting share ownership information are: Fletcher Spaght Ventures II, FSV II and FSV II-B. Fletcher Spaght Ventures is affiliated with Linda Tufts, a member of our board of directors.

**Restricted Stock Agreement with Hatteras**

In February 2015, we entered into a restricted stock agreement with Hatteras Venture Partners which, along with its affiliated entities, is a beneficial owner of greater than 5% of our capital stock, pursuant to which we issued 16,572 shares of Series B redeemable convertible preferred stock to HVP III and 1,504 shares of Series B redeemable convertible preferred stock to HV Affiliates as consideration for certain business development services and services performed or to be performed by Clay B. Thorp as the chairman of our board of directors. Mr. Thorp co-founded and serves as the general partner of Hatteras Venture Partners.

**Investor Rights Agreement**

We have entered into an investor rights agreement, which was amended and restated in August 2018, setting forth voting rights, information rights, rights of co-sale and first refusal and registration rights, among other things, with certain holders of our preferred and common stock. In addition, as described in "Management—Board Composition," the investor rights agreement entitles certain holders of our capital stock to designate directors to our board. Such rights granted under our investor rights agreement will terminate upon the closing of this offering, except that the registration rights granted under our investor rights agreement, as more fully described in "Description of Capital Stock—Registration Rights," will survive this offering.

**Indemnification Agreements**

We plan to enter into indemnification agreements with each of our directors and executive officers in connection with this offering. The indemnification agreements and our amended and restated bylaws, each to be in effect upon the closing of this offering, require us to indemnify our directors and executive officers to the fullest extent permitted by Delaware law. For more information regarding these agreements, see "Executive Compensation—Limitations on Liability and Indemnification Matters."

**Offer Letters and Stock Option Grants to Executive Officers**

We have entered into offer letters with, and granted stock options to, our named executive officers as more fully described in the section entitled "Executive Compensation."

**Related Person Transaction Policy**

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

Under the policy, if a transaction has been identified as a related person transaction, including any transaction that was not a related person transaction when originally consummated or any transaction that was not initially identified as a related person transaction prior to consummation, our management must present information regarding the related person transaction to our audit committee, or, if audit committee approval would be inappropriate, to another independent body of our board of directors, for review, consideration and approval or ratification. The presentation must include a description of, among other things, the material facts, the interests, direct and indirect, of the related persons, the benefits to us of the transaction and whether the transaction is on terms that are comparable to the terms available to or from, as the case may be, an unrelated third party or to or from employees generally. Under the policy, we will collect information that we deem

reasonably necessary from each director, executive officer and, to the extent feasible, significant stockholder to enable us to identify any existing or potential related-person transactions and to effectuate the terms of the policy.

In addition, under our Code of Conduct, which we have adopted in connection with this offering, our employees and directors have an affirmative responsibility to disclose any transaction or relationship that reasonably could be expected to give rise to a conflict of interest.

In considering related person transactions, our audit committee, or other independent body of our board of directors, will take into account the relevant available facts and circumstances including, but not limited to:

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

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

All of the transactions described above were entered into prior to the adoption of the written policy, but all were approved by our board of directors considering similar factors to those described above.

## PRINCIPAL STOCKHOLDERS

The following table sets forth the beneficial ownership of our common stock as of September 30, 2018 and as adjusted to reflect the sale of common stock offered by us in this offering, for:

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

The percentage ownership information shown in the table prior to this offering is based upon 14,683,886 shares of common stock outstanding as of September 30, 2018. The percentage ownership information shown in the table after this offering is based upon 19,683,886 shares of common stock outstanding as of September 30, 2018, assuming the sale of 5,000,000 shares of common stock by us in the offering and no exercise of the underwriters' over-allotment option.

We have determined beneficial ownership in accordance with the rules of the SEC. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities. In addition, the rules include shares of common stock issuable pursuant to the exercise of stock options or warrants that are either immediately exercisable or exercisable on or before November 29, 2018, which is 60 days after September 30, 2018. These shares are deemed to be outstanding and beneficially owned by the person holding those options or warrants for the purpose of computing the percentage ownership of that person, but they are not treated as outstanding for the purpose of computing the percentage ownership of any other person. The information contained in the following table is not necessarily indicative of beneficial ownership for any other purpose, and the inclusion of any shares in the table does not constitute an admission of beneficial ownership of those shares. Unless otherwise indicated, the persons or entities identified in this table have sole voting and investment power with respect to all shares shown as beneficially owned by them, subject to applicable community property laws.

Certain of our existing stockholders, including entities affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of approximately $25.0 million in shares of our common stock in this offering at the initial public offering price per share. Based on an assumed initial public offering price of $13.00 per share, these persons and entities would purchase an aggregate of approximately 2,000,000 of the 5,000,000 shares in this offering based on these indications of interest. However, because indications of interest are not binding agreements or commitments to purchase, the underwriters may determine to sell more, less or no shares in this offering to any of these persons or entities, or any of these persons or entities may determine to purchase more, less or no shares in this offering. The following table does not reflect any potential purchases by these persons or entities or their affiliated entities.

Except as otherwise noted below, the address for persons listed in the table is c/o PhaseBio Pharmaceuticals, Inc., 1 Great Valley Parkway, Suite 30, Malvern, Pennsylvania 19355.

| Name of Beneficial Owner | Number of Shares Beneficially Owned | Percentage of Shares Beneficially Owned | |
|---|---|---|---|
| | | Prior to the Offering (%) | After the Offering (%) |
| *5% or greater stockholders:* | | | |
| Entities affiliated with New Enterprise Associates [1] | 4,849,230 | 33.0 | 24.6 |
| Zeneca, Inc. [2] | 2,407,288 | 16.4 | 12.2 |
| Entities affiliated with Hatteras Venture Partners [3] | 2,169,414 | 14.8 | 11.0 |
| Johnson & Johnson Innovation – JJDC, Inc. [4] | 1,482,933 | 10.1 | 7.5 |
| Entities affiliated with Fletcher Spaght Ventures [5] | 919,965 | 6.3 | 4.7 |
| *Named executive officers and directors:* | | | |
| Jonathan P. Mow [6] | 363,950 | 2.4 | 1.8 |
| John Sharp [7] | 92,835 | * | * |
| John Lee, M.D., Ph.D. [8] | 96,224 | * | * |
| Clay B. Thorp [9] | 2,181,213 | 14.9 | 11.1 |
| Nancy J. Hutson, Ph.D. | — | — | — |
| Peter Justin Klein, M.D., J.D. [10] | 2,306 | * | * |
| Bibhash Mukhopadhyay, Ph.D. | — | — | — |
| Caroline Loewy | — | — | — |
| Tyrell Rivers, Ph.D. | — | — | — |
| Linda Tufts [5] | 919,965 | 6.3 | 4.7 |
| All current executive officers and directors as a group (14 persons) [11] | 3,802,909 | 24.8 | 18.7 |

* Represents beneficial ownership of less than 1%.

(1) Consists of (a) 3,231,774 shares of Series B redeemable convertible preferred stock held directly by NEA 13, (b) 2,070 shares of Series B redeemable convertible preferred stock held directly by NEA Ventures 2009, L.P., or NEA 2009, (c) 260,865 shares of Series C-1 redeemable convertible preferred stock held directly by NEA 13, (d) 1,124,301 shares of Series D redeemable convertible preferred stock held directly by NEA 13, (e) 49,030 shares of Series B redeemable convertible preferred stock issuable upon the exercise of warrants held directly by NEA 13 and (f) 181,190 shares of Series C-1 redeemable convertible preferred stock issuable upon the exercise of warrants held directly by NEA 13. The securities held directly by NEA 2009 are indirectly held by Karen P. Welsh, the general partner of NEA 2009, and the securities held by NEA 13 are indirectly held by (i) NEA Partners 13, L.P., or Partners 13, the sole general partner of NEA 13; (ii) NEA 13 GP, LTD, or NEA 13 LTD, the sole general partner of Partners 13; and (iii) each of the individual directors of NEA 13 LTD. The individual directors of NEA 13 LTD, or the NEA 13 Directors, are M. James Barrett, Peter J. Barris, Forest Baskett, Patrick J. Kerins, David M. Mott, Scott D. Sandell and Ravi Viswanathan. Karen P. Welsh holds voting and dispositive power with regard to the securities held by NEA 2009. NEA Partners 13, NEA 13 LTD and the NEA 13 Directors share voting and dispositive power with regard to the securities owned directly by NEA 13.

The principal business address for all entities and individuals affiliated with New Enterprise Associates is 2855 Sand Hill Road, Menlo Park, CA, 94025.

(2) Consists of (a) 1,553,060 shares of Series C-1 redeemable convertible preferred stock held directly by Zeneca, Inc., (b) 740,337 shares of Series D redeemable convertible preferred stock held directly by Zeneca, Inc. and (c) 113,891 shares of Series C-1 redeemable convertible preferred stock issuable upon the exercise of warrants held directly by Zeneca, Inc. Zeneca, Inc. is a wholly-owned subsidiary of AstraZeneca. The individual directors of AstraZeneca are Pascal Soriot, Marc Dunoyer, Leif Johansson, Rudy Markham, Geneviève Berger, Philip Broadley, Graham Chipchase, Deborah DiSanzo, Sheri McCoy, Nazneen Rahman, Shriti Vadera and Marcus Wallenberg, or the AZ Directors. The securities held directly by Zeneca, Inc. are indirectly held by AstraZeneca and the AZ Directors. AstraZeneca and the AZ Directors have shared voting and dispositive power over the securities and AstraZeneca may be deemed to indirectly beneficially own the securities.

The principal business address for Zeneca, Inc. is 1800 Concord Pike, Wilmington, DE, 19850.

(3) Consists of (a) 52,690 shares of Series 1 redeemable convertible preferred stock held directly by Hatteras Venture Partners I, LP, or HVP I, (b) 42,530 shares of Series 1 redeemable convertible preferred stock held directly by HVP III, (c) 3,862 shares of Series 1 redeemable convertible preferred stock tock held directly by HV Affiliates, (d) 4,846 shares of Series 1 redeemable convertible preferred

stock held directly by Catalysta Ventures, LLC, or Catalysta, (e) 174,699 shares of Series AA redeemable convertible preferred stock held directly by HVP III, (f) 13,609 shares of Series AA redeemable convertible preferred stock held directly by HV Affiliates, (g) 1,026,161 shares of Series B redeemable convertible preferred stock held directly by HVP III, (h) 93,185 shares of Series B redeemable convertible preferred stock held directly by HV Affiliates, (i) 103,001 shares of Series C-1 redeemable convertible preferred stock held directly by HVP III, (j) 9,353 shares of Series C-1 redeemable convertible preferred stock held directly by HV Affiliates, (k) 272,107 shares of Series D redeemable convertible preferred stock held directly by HVP III, (l) 24,709 shares of Series D redeemable convertible preferred stock held directly by HV Affiliates, (m) 226,061 shares of Series D redeemable convertible preferred stock held directly by Multiplier Fund, (n) 26,971 shares of Series B redeemable convertible preferred stock issuable upon the exercise of warrants held directly by HVP III, (o) 2,449 shares of Series B redeemable convertible preferred stock issuable upon the exercise of warrants held directly by HV Affiliates, (p) 47,458 shares of Series C-1 redeemable convertible preferred stock issuable upon the exercise of warrants held directly by HVP III, (q) 4,309 shares of Series C-1 redeemable convertible preferred stock issuable upon the exercise of warrants held directly by HV Affiliates and (r) 41,414 shares of Series C-1 redeemable convertible preferred stock issuable upon the exercise of warrants held directly by Multiplier Fund. Hatteras Venture Advisors III, LLC, or HVA III, is the general partner of HVP I, HVP III, HV Affiliates, Multiplier Fund and Catalysta. The securities held directly by HVP I, HVP III, HV Affiliates and Multiplier Fund are indirectly held by HVA III. The individual general partners of HVA III are Clay B. Thorp, Robert A. Ingram, Kenneth B. Lee, Douglas Reed, MD and John Crumpler, or the GP Directors. HVA III and the GP Directors may share voting and dispositive power with regard to the securities directly held by HVP I, HVP III, HV Affiliates, Multiplier Fund, and Catalysta.

The principal business address for all entities and individuals affiliated with Hatteras Venture Partners is 80 S. Mangum Street, Suite 350 Durham, North Carolina 27701.

(4) Consists of (a) 188,308 shares of Series AA redeemable convertible preferred stock held directly by Johnson & Johnson Innovation—JJDC, Inc., or JJDC, (b) 860,253 shares of Series B redeemable convertible preferred stock held directly by JJDC, (c) 85,280 shares of Series C-1 redeemable convertible preferred stock held directly by JJDC, (d) 283,022 shares of Series D redeemable convertible preferred stock held directly by JJDC, (e) 24,656 shares of Series B redeemable convertible preferred stock issuable upon the exercise of warrants held directly by JJDC and (f) 41,414 shares of Series C-1 redeemable convertible preferred stock issuable upon the exercise of warrants held directly by JJDC. JJDC is a wholly-owned subsidiary of Johnson & Johnson, or J&J. The securities directly held by JJDC are indirectly held by J&J. The individual directors of J&J are Mary C. Beckerle, D. Scott Davis, Ian E.L. Davis, Jennifer A. Doudna, Alex Gorsky, Mark B. McClellan, Anne M. Mulcahy, William D. Perez, Charles Prince, A. Eugene Washington and Ronald A. Williams, or the J&J Directors. J&J and the J&J Directors have shared voting and dispositive power with regard to the securities owned directly by JJDC.

The principal business address of JJDC is 410 George Street, New Brunswick, NJ 08901.

(5) Consists of (a) 119,408 shares of Series AA redeemable convertible preferred stock held directly by Fletcher Spaght Ventures II, (b) 12,025 shares of Series AA redeemable convertible preferred stock held directly by FSV II, (c) 56,874 shares of Series AA redeemable convertible preferred stock held directly by FSV II-B, (d) 340,367 shares of Series B redeemable convertible preferred stock held directly by Fletcher Spaght Ventures II, (e) 34,276 shares of Series B redeemable convertible preferred stock held directly by FSV II, (f) 162,117 shares of Series B redeemable convertible preferred stock held directly by FSV II-B, (g) 37,530 shares of Series C-1 redeemable convertible preferred stock held directly by Fletcher Spaght Ventures II, (h) 3,779 shares of Series C-1 redeemable convertible preferred stock held directly by FSV II, (i) 17,875 shares of Series C-1 redeemable convertible preferred stock held directly by FSV II-B, (j) 63,688 shares of Series D redeemable convertible preferred stock held directly by Fletcher Spaght Ventures II, (k) 6,413 shares of Series D redeemable convertible preferred stock held directly by FSV II, (l) 30,334 shares of Series D redeemable convertible preferred stock held directly by FSV II-B, (m) 12,525 shares of Series B redeemable convertible preferred stock issuable upon the exercise of warrants held directly by Fletcher Spaght Ventures II, (n) 1,261 shares of Series B redeemable convertible preferred stock issuable upon the exercise of warrants held directly by FSV II, (o) 5,965 shares of Series B redeemable convertible preferred stock issuable upon the exercise of warrants held directly by FSV II-B, (p) 9,847 shares of Series C-1 redeemable convertible preferred stock issuable upon the exercise of warrants held directly by Fletcher Spaght Ventures II, (q) 991 shares of Series C-1 redeemable convertible preferred stock issuable upon the exercise of warrants held directly by FSV II and (r) 4,690 shares of Series C-1 redeemable convertible preferred stock issuable upon the exercise of warrants held directly by FSV II-B. FSA II, LLC, or FSA II, is the general partner of the general partner of Fletcher Spaght Ventures II and FSV II-B and the manager of the general partner of FSV II, LP. The members of FSA II are R. John Fletcher, Pearson M. Spaght and Linda Tufts, or the FSA II Members. FSA II and the FSA II members may share voting and dispositive power with regard to the securities owned directly by Fletcher Spaght Ventures II, FSV II-B, and FSV II.

The principal business address for all entities and individuals affiliated with Fletcher Spaght Ventures is 222 Berkeley Street Boston, MA 02116.

(6) Consists of (a) 45,194 shares of common stock held by the Mow Trust dated April 17, 2008, (b) 3,505 shares of Series B redeemable convertible preferred stock held by the Mow Trust dated April 17, 2008, (c) 310 shares of Series B redeemable convertible preferred stock issuable upon the exercise of warrants and (d) 314,941 shares of common stock issuable upon the exercise of options. Mr. Mow and his wife Diana Mow are joint trustees of the Mow Trust dated April 17, 2008 and share voting and dispositive power for such shares.

(7) Consists of 92,835 shares of common stock issuable upon the exercise of options.

(8) Consists of 96,224 shares of common stock issuable upon the exercise of options.

(9) Consists of 11,799 shares of common stock held by Mr. Thorp. Also consists of (a) 52,690 shares of Series 1 redeemable convertible preferred stock held directly by Hatteras Venture Partners I, LP, or HVP I, (b) 42,530 shares of Series 1 redeemable convertible preferred stock held directly by HVP III, (c) 3,862 shares of Series 1 redeemable convertible preferred stock tock held directly by HV Affiliates, (d) 4,846 shares of Series 1 redeemable convertible preferred stock held directly by Catalysta Ventures, LLC, or Catalysta, (e) 174,699 shares of Series AA redeemable convertible preferred stock held directly by HVP III, (f) 13,609 shares of Series AA redeemable convertible preferred stock held directly by HV Affiliates, (g) 1,026,161 shares of Series B redeemable convertible preferred stock held directly by HVP III, (h) 93,185 shares of Series B redeemable convertible preferred stock held directly by HV Affiliates, (i) 103,001 shares of Series C-1 redeemable convertible preferred stock held directly by HVP III, (j) 9,353 shares of Series C-1 redeemable convertible preferred stock held directly by HV Affiliates, (k) 272,107 shares of Series D redeemable convertible preferred stock held directly by HVP III, (l) 24,709 shares of Series D redeemable convertible preferred stock held directly by HV Affiliates, (m) 226,061 shares of Series D redeemable convertible preferred stock held directly by Multiplier Fund, (n) 26,971 shares of Series B redeemable convertible preferred stock issuable upon the exercise of warrants held directly by HVP III, (o) 2,449 shares of Series B redeemable convertible preferred stock issuable upon the exercise of warrants held directly by HV Affiliates, (p) 47,458 shares of Series C-1 redeemable convertible preferred stock issuable upon the exercise of warrants held directly by HVP III, (q) 4,309 shares of Series C-1 redeemable convertible preferred stock issuable upon the exercise of warrants held directly by HV Affiliates and (r) 41,414 shares of Series C-1 redeemable convertible preferred stock issuable upon the exercise of warrants held directly by Multiplier Fund. HVA III is the general partner of HVP I, HVP III, HV Affiliates and Multiplier Fund. HVA III is the general partner of HVP I, HVP III, HV Affiliates, Multiplier Fund and Catalysta. The securities held directly by HVP I, HVP III, HV Affiliates and Multiplier Fund are indirectly held by HVA III. The individual general partners of HVA III are Clay B. Thorp, Robert A. Ingram, Kenneth B. Lee, Douglas Reed, MD and John Crumpler, or the GP Directors. HVA III and the GP Directors may share voting and dispositive power with regard to the securities directly held by HVP I, HVP III, HV Affiliates, Multiplier Fund and Catalysta. Mr. Thorp is a manager of Catalysta and may share voting and dispositive power with regard to the securities held directly by Catalysta.

(10) Consists of (a) 2,203 shares of Series B redeemable convertible preferred stock and (b) 103 shares of Series B redeemable convertible preferred stock issuable upon the exercise of warrants.

(11) Consists of (a) 56,993 shares of common stock, (b) 103,928 shares of Series 1 redeemable convertible preferred stock, (c) 376,615 shares of Series AA redeemable convertible preferred stock, (d) 1,664,017 shares of Series B redeemable convertible preferred stock, (e) 171,538 shares of Series C-1 redeemable convertible preferred stock, (f) 623,312 shares of Series D redeemable convertible preferred stock, (g) 49,687 shares of Series B redeemable convertible preferred stock issuable upon the exercise of warrants, (h) 108,709 shares of Series C-1 redeemable convertible preferred stock issuable upon the exercise of warrants and (i) 648,110 shares of common stock issuable upon the exercise of options.

## DESCRIPTION OF CAPITAL STOCK

The following descriptions of our capital stock, certain provisions of our amended and restated certificate of incorporation and amended and restated bylaws, as each will be in effect upon the closing of this offering, and certain provisions of Delaware law are summaries. You should also refer to the amended and restated certificate of incorporation and the amended and restated bylaws, which are filed as exhibits to the registration statement of which this prospectus is a part. We refer in this section to our amended and restated certificate of incorporation and amended and restated bylaws that we intend to adopt in connection with this offering as our certificate of incorporation and bylaws, respectively.

### General

Upon the completion of this offering, our amended and restated certificate of incorporation will authorize us to issue up to 200,000,000 shares of common stock, $0.001 par value per share, and 10,000,000 shares of preferred stock, $0.001 par value per share, all of which shares of preferred stock will be undesignated. Our board of directors may establish the rights and preferences of the preferred stock from time to time.

As of June 30, 2018, there were outstanding 745,788 shares of our common stock held by 50 stockholders of record. After giving effect to the automatic conversion of all outstanding shares of our redeemable convertible preferred stock into 13,064,781 shares of common stock in connection with the closing of this offering, there would have been 13,810,569 shares of common stock issued and outstanding, held by 70 stockholders of record.

### Common Stock

#### *Voting Rights*

Each holder of our common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. Under our amended and restated certificate of incorporation and amended and restated bylaws, which will become effective in connection with the closing of this offering, our stockholders will not have cumulative voting rights. Because of this, the holders of a majority of the shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they should so choose.

#### *Dividends*

Subject to preferences that may be applicable to any then-outstanding preferred stock, holders of common stock are entitled to receive ratably those dividends, if any, as may be declared from time to time by the board of directors out of legally available funds.

#### *Liquidation*

In the event of our liquidation, dissolution or winding up, holders of common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then-outstanding shares of preferred stock.

#### *Rights and Preferences*

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

### Stock Options

As of June 30, 2018, options to purchase an aggregate of 1,210,776 shares of common stock were outstanding at a weighted-average exercise price of $1.68 per share. For additional information regarding the terms of our 2002 Plan, see “Executive Compensation—Equity Incentive Plans—Amended and Restated 2002 Stock Plan.”

**Warrants**

As of June 30, 2018, there were outstanding warrants to purchase an aggregate of 130,740 shares of Series B redeemable convertible preferred stock at a weighted-average exercise price of $2.01 per share and warrants to purchase an aggregate of 354,110 shares of Series C-1 redeemable convertible preferred stock at a weighted-average exercise price of $1.46 per share. In August 2018, we issued warrants to purchase 368,582 shares of Series C-1 redeemable convertible preferred stock at an exercise price of $0.12. If not earlier exercised, warrants to purchase an aggregate of 104,856 shares of Series B redeemable convertible preferred stock and warrants to purchase an aggregate of 672,979 shares of Series C-1 redeemable convertible preferred stock will expire and no longer be exercisable upon the closing of this offering. After giving effect to the conversion of warrants to purchase preferred stock into warrants to purchase common stock in connection with the closing of this offering, and assuming the exercise of the above warrants, there would have been outstanding warrants to purchase an aggregate of 75,597 shares of common stock at a weighted-average exercise price of $9.659 per share.

**Preferred Stock**

As of June 30, 2018, there were outstanding 132,255 shares of our Series 1 redeemable convertible preferred stock, 1 share of our Series 2 redeemable convertible preferred stock, 573,961 shares of our Series AA redeemable convertible preferred stock, 6,251,502 shares of our Series B redeemable convertible preferred stock and 2,174,280 shares of our Series C-1 redeemable convertible preferred stock. In August 2018, we issued 3,923,168 shares of our Series D redeemable convertible preferred stock.

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

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

We have no present plans to issue any shares of preferred stock following completion of this offering.

**Registration Rights**

After the closing of this offering, certain holders of the common stock, including holders of the shares of our common stock that will be issued upon conversion of our redeemable convertible preferred stock in connection with this offering, will be entitled to certain rights with respect to registration of such shares under the Securities Act pursuant to the terms of an investor rights agreement. These shares are collectively referred to herein as registrable securities.

The investor rights agreement provides the holders of registrable securities with demand, piggyback and S-3 registration rights as described more fully below. As of June 30, 2018, after giving effect to the automatic conversion of all outstanding shares of redeemable convertible preferred stock into 13,064,781 shares of our common stock and the expected exercise of outstanding warrants to purchase 777,835 shares of the Company's redeemable convertible preferred stock in connection with the closing of the offering, there would have been an aggregate of 13,832,226 registrable securities that were entitled to registration rights.

***Demand Registration Rights***

At any time beginning six months after the effective date of the registration statement of which this prospectus forms a part, the holders of at least 60% of the registrable securities then outstanding have the right to make a demand that we file a registration statement under the Securities Act covering registrable securities then outstanding, subject to specified exceptions.

***Piggyback Registration Rights***

If we register any securities for public sale, the holders of our registrable securities then outstanding will each be entitled to notice of the registration and will have the right to include their shares in the registration statement.

The underwriters of any underwritten offering will have the right to limit the number of shares having registration rights to be included in the registration statement, but not below 25% of the total number of securities included in such registration.

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

If we are eligible to file a registration statement on Form S-3, the holders of our registrable securities have the right to demand that we file registration statements on Form S-3; provided, that the aggregate price to the public of the securities to be sold under the registration statement is at least $2.5 million. The right to have such shares registered on Form S-3 is further subject to other specified conditions and limitations.

***Expenses of Registration***

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

***Termination of Registration Rights***

The registration rights will terminate upon the earlier of a liquidation event or a written agreement between us and holders of at least 60% of the outstanding registrable securities. The registration rights will terminate with respect to any particular stockholder when such stockholder (a) is able to sell all of its shares pursuant to Rule 144 under the Securities Act or (b) holds one percent or less of our common stock and such stockholder is able to sell all registrable securities during a 90-day period pursuant to Rule 144 under the Securities Act.

**Anti-Takeover Provisions**

***Section 203 of the Delaware General Corporation Law***

We are subject to Section 203 of the Delaware General Corporation Law, which prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years after the date that such stockholder became an interested stockholder, with the following exceptions:

- before such date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction began, excluding for purposes of determining the voting stock outstanding, but not the outstanding voting stock owned by the interested stockholder, those shares owned (1) by persons who are directors and also officers and (2) employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

- on or after such date, the business combination is approved by the board of directors and authorized at an annual or special meeting of the stockholders, and not by written consent, by the affirmative vote of at least 66⅔% of the outstanding voting stock that is not owned by the interested stockholder.

In general, Section 203 defines a "business combination" to include the following:

- any merger or consolidation involving the corporation or any direct or indirect majority-owned subsidiary of the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder (in one transaction or a series of transactions);
- subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation or by any direct or indirect majority-owned subsidiary of the corporation of any stock of the corporation or of such subsidiary to the interested stockholder;
- any transaction involving the corporation or any direct or indirect majority-owned subsidiary of the corporation that has the effect of increasing the proportionate share of the stock or any class or series of the corporation beneficially owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits by or through the corporation.

In general, Section 203 defines an "interested stockholder" as an entity or person who, together with the person's affiliates and associates, beneficially owns, or within three years prior to the time of determination of interested stockholder status did own, 15% or more of the outstanding voting stock of the corporation.

***Certificate of Incorporation and Bylaws to be in Effect Upon the Closing of this Offering***

Our amended and restated certificate of incorporation to be in effect upon the completion of this offering, or our restated certificate, will provide for our board of directors to be divided into three classes with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. Because our stockholders do not have cumulative voting rights, stockholders holding a majority of the shares of common stock outstanding will be able to elect all of our directors. Our restated certificate and our amended and restated bylaws to be effective upon the completion of this offering, or our restated bylaws, will also provide that directors may be removed by the stockholders only for cause upon the vote of 66 $^{2}/_{3}$% or more of our outstanding common stock. Furthermore, the authorized number of directors may be changed only by resolution of the board of directors, and vacancies and newly created directorships on the board of directors may, except as otherwise required by law or determined by the board of directors, only be filled by a majority vote of the directors then serving on the board of directors, even though less than a quorum.

Our restated certificate and restated bylaws will also provide that all stockholder actions must be effected at a duly called meeting of stockholders and will eliminate the right of stockholders to act by written consent without a meeting. Our restated bylaws will also provide that only our Chairman of the board of directors, Chief Executive Officer or the board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors may call a special meeting of stockholders.

Our restated bylaws will also provide that stockholders seeking to present proposals before a meeting of stockholders to nominate candidates for election as directors at a meeting of stockholders must provide timely advance notice in writing, and will specify requirements as to the form and content of a stockholder's notice.

Our restated certificate and restated bylaws will provide that the stockholders cannot amend many of the provisions described above except by a vote of 66 $^{2}/_{3}$% or more of our outstanding common stock. As described in "—Preferred Stock" above, our restated certificate will give our board of directors the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series.

The combination of these provisions will make it more difficult for our existing stockholders to replace our board of directors as well as for another party to obtain control of us by replacing our board of directors. Since our board of directors has the power to retain and discharge our officers, these provisions could also make it more difficult for existing stockholders or another party to effect a change in management. In addition, the authorization of undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change our control.

These provisions are intended to enhance the likelihood of continued stability in the composition of our board of directors and its policies and to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to reduce our vulnerability to hostile takeovers and to discourage certain tactics that may be used in proxy fights. However, such provisions could have the effect of discouraging others from making tender offers for our shares and may have the effect of delaying changes in our control or management. As a consequence, these provisions may also inhibit fluctuations in the market price of our stock that could result from actual or rumored takeover attempts. We believe that the benefits of these provisions, including increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure our company, outweigh the disadvantages of discouraging takeover proposals, because negotiation of takeover proposals could result in an improvement of their terms.

**Choice of Forum**

Our amended and restated certificate of incorporation will provide that the Court of Chancery of the State of Delaware will be the exclusive forum for:

- any derivative action or proceeding brought on our behalf;
- any action asserting a breach of fiduciary duty;
- any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our restated certificate, or our amended and restated bylaws; or
- any action asserting a claim against us that is governed by the internal affairs doctrine.

The provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act. In addition, our amended and restated bylaws will also provide that unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act.

The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any action, a court could find the choice of forum provisions contained in our restated certificate to be inapplicable or unenforceable in such action.

Our restated certificate will further provide 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.

**Transfer Agent and Registrar**

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A. The transfer agent's address is 250 Royall Street, Canton, Massachusetts 02021.

**Listing**

We have applied for listing of our common stock on the Nasdaq Global Market under the symbol "PHAS."

## SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, no public market existed for our capital stock, and although we expect that our common stock will be approved for listing on the Nasdaq Global Market, we cannot assure investors that there will be an active public market for our common stock following this offering. We cannot predict what effect, if any, sales of our shares in the public market or the availability of shares for sale will have on the market price of our common stock. Future sales of substantial amounts of common stock in the public market, the availability of shares for future sale or the perception that such sales may occur, however, could adversely affect the market price of our common stock and also could adversely affect our future ability to raise capital through the sale of our common stock or other equity-related securities at times and prices we believe appropriate.

Based on our shares outstanding as of June 30, 2018, upon the closing of this offering, 19,588,404 shares of our common stock will be outstanding, or 20,338,404 shares of common stock if the underwriters exercise their over-allotment option in full, in each case assuming no outstanding options or warrants are exercised.

All of the shares of common stock sold in this offering will be freely tradable without restrictions or further registration under the Securities Act, except for any shares sold to our "affiliates," as that term is defined under Rule 144 under the Securities Act. The outstanding shares of common stock held by existing stockholders are "restricted securities," as that term is defined in Rule 144 under the Securities Act. Restricted securities may be sold in the public market only if the offer and sale is registered under the Securities Act or if the offer and sale of those securities qualifies for exemption from registration, including exemptions provided by Rules 144 or 701 promulgated under the Securities Act.

As a result of lock-up agreements and market standoff provisions described below and the provisions of Rules 144 and 701, shares of our common stock will be available for sale in the public market as follows:

- 5,000,000 shares of our common stock will be eligible for immediate sale upon the closing of this offering; and
- approximately 14,588,404 shares of our common stock will be eligible for sale upon expiration of lock-up agreements and market standoff provisions described below, beginning 181 days after the date of this prospectus, subject in certain circumstances to the volume, manner of sale and other limitations under Rule 144 and Rule 701.

We may issue shares of our capital stock from time to time for a variety of corporate purposes, including in capital-raising activities through future public offerings or private placements, in connection with the exercise of stock options and warrants, vesting of restricted stock units and other issuances relating to our employee benefit plans and as consideration for future acquisitions, investments or other purposes. The number of shares of our capital stock that we may issue may be significant, depending on the events surrounding such issuances. In some cases, the shares we issue may be freely tradable without restriction or further registration under the Securities Act; in other cases, we may grant registration rights covering the shares issued in connection with these issuances, in which case the holders of the shares will have the right, under certain circumstances, to cause us to register any resale of such shares to the public.

### Rule 144

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

***Non-Affiliates***

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

- the restricted securities have been held for at least six months, including the holding period of any prior owner other than one of our affiliates;
- we have been subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale; and
- we are current in our Exchange Act reporting at the time of sale.

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

***Affiliates***

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

- 1% of the number of shares of our common stock then outstanding, which will equal approximately 195,884 shares immediately after the closing of this offering based on the number of shares outstanding as of June 30, 2018; or
- the average weekly trading volume of our common stock on the Nasdaq Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale.

**Rule 701**

In general, under Rule 701, a person who purchased shares of our common stock pursuant to a written compensatory plan or contract and who is not deemed to have been one of our affiliates during the immediately preceding 90 days may sell these shares in reliance upon Rule 144, but without being required to comply with the holding period, notice, manner of sale, public information requirements or volume limitation provisions of Rule 144. Rule 701 also permits affiliates to sell their Rule 701 shares under Rule 144 without complying with the holding period requirements of Rule 144. All holders of Rule 701 shares, however, are subject to the expiration of the lock-up agreements and market standoff provisions described below.

**Form S-8 Registration Statements**

As of June 30, 2018, options to purchase an aggregate of 1,210,776 shares of our common stock were outstanding. As soon as practicable after the closing of this offering, we intend to file with the SEC one or more registration statements on Form S-8 under the Securities Act to register the shares of our common stock that are issuable pursuant to our equity incentive plans, including pursuant to outstanding options. See “Executive Compensation—Equity Incentive Plans” for a description of our equity incentive plans. These registration statements will become effective immediately upon filing. Shares covered by these registration statements will then be eligible for sale in the public markets, subject to vesting restrictions, any applicable lock-up agreements described below and Rule 144 limitations applicable to affiliates.

**Lock-Up Agreements**

In connection with this offering, we, our directors, our executive officers and holders of all of our outstanding shares of common stock or securities convertible into or exchangeable for shares of our common stock outstanding upon the completion of this offering, have agreed, subject to certain exceptions, with the underwriters for this offering not to directly or indirectly offer, sell, contract to sell, pledge, grant any option to purchase, make any short sale or otherwise dispose of or hedge any shares of our common stock or any options to purchase shares of our common stock, or any securities convertible into or exchangeable for shares of common stock during the period from the date of the lock-up agreement continuing through the date 180 days after the date of this prospectus, except with the prior written consent of Citigroup Global Markets Inc. and Cowen and Company, LLC and certain other exceptions. These agreements are described in the section titled "Underwriting."

Prior to the expiration of the lock-up period described above, certain of our employees, including our executive officers and/or directors may enter into written trading plans that are intended to comply with Rule 10b5-1 under the Exchange Act. Sales under these trading plans would not be permitted until the expiration of the lock-up agreements relating to the offering described above.

**Registration Rights**

Upon the closing of this offering, the holders of 13,832,226 shares of our common stock will be entitled to certain rights with respect to the registration of the offer and sale of their shares under the Securities Act. Registration of the offer and sale of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act immediately upon the effectiveness of the registration. See "Description of Capital Stock—Registration Rights" for additional information.

## MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS

The following summary describes the material U.S. federal income tax consequences of the acquisition, ownership and disposition of our common stock acquired in this offering by Non-U.S. Holders (as defined below). This discussion does not address all aspects of U.S. federal income taxation and does not address any non-U.S., state or local tax consequences that may be relevant to Non-U.S. Holders in light of their particular circumstances, nor does it address U.S. federal tax consequences other than income taxes, such as gift or estate taxes. Rules different from those described below may apply to certain Non-U.S. Holders that are subject to special treatment under the Code such as financial institutions, insurance companies, tax-exempt organizations, broker-dealers and traders in securities, government organizations, certain foreign citizens or long-term residents of the United States, "controlled foreign corporations," "passive foreign investment companies," corporations that accumulate earnings to avoid U.S. federal income tax, persons that hold our common stock as part of a "straddle," "hedge," "conversion transaction," "synthetic security" or integrated investment or other risk reduction strategy, persons subject to the alternative minimum tax or federal Medicare contribution tax on net investment income, persons who have a functional currency other than the U.S. dollar, accrual method taxpayers subject to special tax accounting rules under Section 451(b) of the Code, partnerships and other pass-through entities and investors in such pass-through entities. Such Non-U.S. Holders are urged to consult their own tax advisors to determine the U.S. federal, state, local and other tax consequences that may be relevant to them. Furthermore, the discussion below is based upon the provisions of the Code and Treasury regulations, rulings and judicial decisions promulgated thereunder as of the date hereof, and such authorities may be repealed, revoked or modified, perhaps retroactively, so as to result in U.S. federal income tax consequences different from those discussed below. We have not requested a ruling from the U.S. Internal Revenue Service, or IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions. This discussion assumes that the Non-U.S. Holder holds our common stock as a "capital asset" within the meaning of Section 1221 of the Code (generally, property held for investment).

Persons considering purchasing our common stock pursuant to this offering should consult their own tax advisors concerning the U.S. federal income, estate and other tax consequences of acquiring, owning and disposing of our common stock in light of their particular situations as well as any consequences arising under the laws of any other taxing jurisdiction, including any state, local or non-U.S. tax consequences. You should also consult with your tax advisor with respect to recently enacted changes in U.S. tax law as well as potential conforming changes in state tax laws.

For the purposes of this discussion, a "Non-U.S. Holder" is, for U.S. federal income tax purposes, a beneficial owner of our common stock that is neither a U.S. Holder nor a partnership (or other entity treated as a partnership for U.S. federal income tax purposes regardless of its place of organization or formation). A "U.S. Holder" means a beneficial owner of our common stock that is, for U.S. federal income tax purposes. (1) an individual who is a citizen or resident of the United States, (2) a corporation or other entity treated as a corporation created or organized in or under the laws of the United States., any state thereof or the District of Columbia, (3) an estate the income of which is subject to U.S. federal income taxation regardless of its source or (4) a trust if it (a) is subject to the primary supervision of a court within the United States and one or more U.S. persons have the authority to control all substantial decisions of the trust or (b) has a valid election in effect under applicable Treasury regulations to be treated as a U.S. person.

### Distributions on Our Common Stock

Distributions, if any, made on our common stock to a Non-U.S. Holder to the extent made out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles) generally will constitute dividends for U.S. tax purposes. Subject to the discussion below regarding backup withholding and foreign accounts, such dividends will be subject to withholding tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. To obtain a reduced rate of withholding tax under a treaty, a Non-U.S. Holder generally will be required to provide us with a properly executed IRS Form W-8BEN (in the

case of individuals), IRS Form W-8BEN-E (in the case of entities) or other appropriate form, including a U.S. taxpayer identification number and certifying the Non-U.S. Holder's entitlement to benefits under that treaty. This certification must be provided to us or our paying agent prior to the payment of dividends and must be updated periodically. In the case of a Non-U.S. Holder that is an entity, Treasury regulations and the relevant tax treaty provide rules to determine whether, for purposes of determining the applicability of a tax treaty, dividends will be treated as paid to the entity or to those holding an interest in that entity. If a Non-U.S. Holder holds stock through a financial institution or other agent acting on the holder's behalf, the holder will be required to provide appropriate documentation to such agent. The holder's agent will then be required to provide certification to us or our paying agent, either directly or through other intermediaries. If you are eligible for a reduced rate of U.S. federal withholding tax under an income tax treaty and you do not timely provide the required certification, you may be able to obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim for a refund with the IRS.

We generally are not required to withhold tax on dividends paid to a Non-U.S. Holder that are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, are attributable to a permanent establishment that such holder maintains in the United States) if a properly executed IRS Form W-8ECI, stating that the dividends are so connected, is furnished to us (or, if stock is held through a financial institution or other agent, to such agent). In general, such effectively connected dividends will be subject to U.S. federal income tax, on a net income basis at the regular graduated rates applicable to U.S. residents. A corporate Non-U.S. Holder receiving effectively connected dividends may also be subject to an additional "branch profits tax" which is imposed, under certain circumstances, at a rate of 30% (or such lower rate as may be specified by an applicable treaty) on the corporate Non-U.S. Holder's effectively connected earnings and profits, subject to certain adjustments. Non-U.S. Holders should consult their tax advisors regarding any applicable income tax treaties that may provide for different rules.

To the extent distributions on our common stock, if any, exceed our current and accumulated earnings and profits, they will first reduce the Non-U.S. Holder's adjusted basis in our common stock, but not below zero, and then will be treated as gain to the extent of any excess and taxed in the same manner as gain realized from a sale or other disposition of common stock as described in the next section.

**Gain on Disposition of Our Common Stock**

Subject to the discussion below regarding backup withholding and foreign accounts, a Non-U.S. Holder generally should not be subject to U.S. federal income tax with respect to gain realized on a sale or other disposition of our common stock unless (1) the gain is effectively connected with a trade or business of such holder in the United States (and, if required by an applicable income tax treaty, is attributable to a permanent establishment that such holder maintains in the United States), (2) the Non-U.S. Holder is a nonresident alien individual and is present in the United States for 183 or more days in the taxable year of the disposition and certain other conditions are met or (3) we are or have been a "United States real property holding corporation" within the meaning of Section 897(c)(2) of the Code at any time within the shorter of the five-year period preceding such disposition or such holder's holding period. In general, we would be a U.S. real property holding corporation if interests in U.S. real estate comprised at least half of the fair market value of our business assets. We believe that we are not, and do not anticipate becoming, a U.S. real property holding corporation. However, because the determination of whether we are a U.S. real property holding corporation depends on the fair market value of our U.S. real property relative to the fair market value of our other business assets, there can be no assurance that we will not become a U.S. real property holding corporation in the future. Even if we are treated as a U.S. real property holding corporation, gain realized by a Non-U.S. Holder on a disposition of our common stock will not be subject to U.S. federal income tax so long as (a) the Non-U.S. Holder owned, directly, indirectly and constructively, no more than five percent of our common stock at all times within the shorter of (1) the five-year period preceding the disposition or (2) the holder's holding period and (b) our common stock is regularly traded on an established securities market. There can be no assurance that our common stock will qualify as regularly traded on an established securities market. If any gain on your disposition is taxable because we are a U. S. real property holding corporation and your ownership of our common stock exceeds 5%, you will be taxed

on such disposition generally in the manner applicable to U.S. persons and, in addition, a purchaser of your common stock may be required to withhold tax with respect to that obligation.

If you are a Non-U.S. Holder described in (1) above, you will be required to pay tax on the net gain derived from the sale at regular graduated U.S. federal income tax rates, and corporate Non-U.S. Holders described in (1) above may be subject to the additional branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. If you are an individual Non-U.S. Holder described in (2) above, you will be required to pay a flat 30% tax on the gain derived from the sale, and such gain may be offset by U.S.-source capital losses if you timely file U.S. tax returns reporting the losses (even though you are not considered a resident of the U.S.).

**Information Reporting Requirements and Backup Withholding**

Generally, we must report information to the IRS with respect to any dividends we pay on our common stock (even if the payments are not subject to withholding) including the amount of any such dividends, the name and address of the recipient and the amount, if any, of tax withheld. A similar report is sent to dividend recipients. The IRS may make its reports available to tax authorities in the recipient's country of residence pursuant to tax treaties or certain other agreements.

Dividends paid by us or by our paying agents to a Non-U.S. Holder may also be subject to U.S. backup withholding. U.S. backup withholding generally will not apply to a Non-U.S. Holder who provides a properly executed IRS Form W-8BEN (in the case of individuals) or IRS Form W-8BEN-E (in the case of entities), IRS Form W-8ECI or otherwise establishes an exemption. Notwithstanding the foregoing, backup withholding may apply if the payor has actual knowledge, or reason to know, that the holder is a U.S. person who is not an exempt recipient.

Under current U.S. federal income tax law, U.S. information reporting and backup withholding requirements generally will apply to the proceeds of a disposition of our common stock effected by or through a U.S. office of any broker, U.S. or foreign, except that information reporting and such requirements may be avoided if the holder provides a properly executed IRS Form W-8BEN (in the case of individuals) or IRS Form W-8BEN-E (in the case of entities) or otherwise satisfies documentary evidence requirements for establishing Non- U.S. Holder status or otherwise establishes an exemption. Generally, U.S. information reporting and backup withholding requirements will not apply to a payment of disposition proceeds to a Non-U.S. Holder where the transaction is effected outside the U.S. through a non-U.S. office of a non-U.S. broker. Information reporting and backup withholding requirements may, however, apply to a payment of disposition proceeds if the broker has actual knowledge, or reason to know, that the holder is, in fact, a U.S. person. For information reporting purposes, certain brokers with substantial U.S. ownership or operations will generally be treated in a manner similar to U.S. brokers.

Any amounts of tax withheld under the backup withholding rules may be credited against the tax liability of persons subject to backup withholding, provided that the required information is timely furnished to the IRS.

**Foreign Accounts**

A U.S. federal withholding tax of 30% may apply to dividends on and the gross proceeds of a disposition of our common stock paid to a foreign financial institution (as specifically defined by applicable rules), unless such institution enters into an agreement with the U.S. government to withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding U.S. account holders of such institution (which includes certain equity holders of such institution, as well as certain account holders that are foreign entities with U.S. owners). This U.S. federal withholding tax of 30% will also apply to dividends on and the gross proceeds of a disposition of our common stock to a non-financial foreign entity, unless such entity provides the withholding agent with either a certification that it does not have any substantial direct or indirect U.S. owners or provides information regarding substantial direct and indirect U.S. owners of the entity. The withholding tax described above will not apply if the foreign financial institution or non-financial foreign entity

otherwise qualifies for an exemption from the rules. Under certain circumstances, a Non-U.S. Holder might be eligible for refunds or credits of such taxes. Holders are encouraged to consult with their own tax advisors regarding the possible implications of these rules to their investment in our common stock.

The withholding provisions described above apply currently to payments of dividends and will apply to payments of gross proceeds from a sale or other disposition of common stock on or after January 1, 2019.

EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS OWN TAX ADVISOR REGARDING THE TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY RECENT AND PROPOSED CHANGE IN APPLICABLE LAW.

## UNDERWRITING

Citigroup Global Markets Inc., Cowen and Company, LLC and Stifel, Nicolaus & Company, Incorporated are acting as book-running managers of this offering and as representatives of the underwriters named below. Subject to the terms and conditions stated in the underwriting agreement dated the date of this prospectus, the underwriters named below have severally agreed to purchase, and we have agreed to sell to them, the number of shares of our common stock indicated below:

| Underwriter | Number of Shares |
|---|---|
| Citigroup Global Markets Inc. | |
| Cowen and Company, LLC | |
| Stifel, Nicolaus & Company, Incorporated | |
| Needham & Company, LLC | |
| Total | 5,000,000 |

The underwriting agreement provides that the obligations of the underwriters to purchase the shares of our common stock included in this offering are subject to approval of legal matters by counsel and to other conditions. The underwriters are obligated to purchase all of the shares of our common stock (other than those covered by the over-allotment option described below) if they purchase any of the shares.

Shares of our common stock sold by the underwriters to the public will initially be offered at the initial public offering price set forth on the cover of this prospectus. Any shares of our common stock sold by the underwriters to securities dealers may be sold at a discount from the initial public offering price not to exceed $ per share. After the initial public offering of the shares of our common stock, if all the shares of our common stock are not sold at the initial public offering price, the underwriters may change the offering price and the other selling terms. The representatives have advised us that the underwriters do not intend to make sales to discretionary accounts.

If the underwriters sell more shares of our common stock than the total number set forth in the table above, we have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to additional shares of our common stock at the initial public offering price less the underwriting discount. The underwriters may exercise the option solely for the purpose of covering over-allotments, if any, in connection with this offering. To the extent the option is exercised, each underwriter must purchase a number of additional shares of our common stock approximately proportionate to that underwriter's initial purchase commitment set forth in the table above. Any shares of our common stock issued or sold under the option will be issued and sold on the same terms and conditions as the other shares of our common stock that are the subject of this offering.

We, our officers and directors and all of our stockholders have agreed that, subject to specified limited exceptions, for a period of 180 days from the date of this prospectus, we and they will not, without the prior written consent of Citigroup Global Markets Inc. and Cowen and Company, LLC, offer, sell, contract to sell, pledge or otherwise dispose of, including the filing of a registration statement in respect of, or hedge any shares of our common stock or any securities convertible into, or exercisable or exchangeable for, our common stock. Citigroup Global Markets Inc. and Cowen and Company, LLC in their sole discretion may release any of the securities subject to these lock-up agreements at any time, which, in the case of officers and directors, shall be with notice.

Prior to this offering, there has been no public market for our common stock. Consequently, the initial public offering price for the shares of our common stock will be determined by negotiations between us and the representatives. Among the factors considered in determining the initial public offering price will be our results of operations, our current financial condition, our future prospects, our markets, the economic conditions in and future prospects for the industry in which we compete, our management, and currently prevailing general

conditions in the equity securities markets, including current market valuations of publicly traded companies considered comparable to our company. We cannot assure you, however, that the price at which the shares of our common stock will sell in the public market after this offering will not be lower than the initial public offering price or that an active trading market in our shares of common stock will develop and continue after this offering.

We have applied for listing of our common stock listed on the Nasdaq Global Market under the symbol "PHAS."

The following table shows the per share and total public offering price, underwriting discounts and commissions that we are to pay to the underwriters and proceeds to us, before expenses, in connection with this offering. These amounts are shown assuming both no exercise and full exercise of the underwriters' over-allotment option:

| | | Total | |
|---|---|---|---|
| | **Per share** | **No exercise** | **Full exercise** |
| Public offering price | $ | $ | $ |
| Underwriting discounts and commissions paid by us | $ | $ | $ |
| Proceeds to us, before expenses | $ | $ | $ |

We estimate that expenses payable by us in connection with this offering, exclusive of underwriting discounts and commissions, will be approximately $2,550,000. We have also agreed to reimburse the underwriters for expenses in an amount up to $30,000 relating to the clearance of this offering with the Financial Industry Regulatory Authority, Inc.

In connection with this offering, the underwriters may purchase and sell shares of our common stock in the open market. Purchases and sales in the open market may include short sales, purchases to cover short positions, which may include purchases pursuant to the underwriters' over-allotment option, and other transactions that would stabilize, maintain or otherwise affect the price of our common stock.

- Short sales involve secondary market sales by the underwriters of a greater number of shares of our common stock than they are required to purchase in this offering:
    - "Covered" short sales are sales of shares of our common stock in an amount up to the number of shares of our common stock represented by the underwriters' over-allotment option.
    - "Naked" short sales are sales of shares of our common stock in an amount in excess of the number of shares of our common stock represented by the underwriters' over-allotment option.
- The underwriters can close out a short position by purchasing additional shares of our common stock, either pursuant to the underwriters' over-allotment option or in the open market.
    - To close a naked short position, the underwriters must purchase shares of our common stock in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.
    - To close a covered short position, the underwriters must purchase shares of our common stock in the open market or exercise their over-allotment option. In determining the source of shares of our common stock to close the covered short position, the underwriters will consider, among other things, the price of shares of our common stock available for purchase in the open market as compared to the price at which they may purchase shares of our common stock through their over-allotment option.
- As an additional means of facilitating this offering, the underwriters may bid for, and purchase, shares of our common stock on the Nasdaq Global Market, as long as such bids do not exceed a specified maximum, to stabilize the price of the shares of our common stock.

Purchases to cover short positions and stabilizing purchases, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of the shares. They may also cause the price of the shares of our common stock to be higher than the price that would otherwise prevail in the open market in the absence of these transactions. The underwriters may conduct these transactions on the Nasdaq Global Market, in the over-the-counter market or otherwise. The underwriters are not required to engage in any of these transactions and may discontinue them at any time.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make because of any of those liabilities.

A prospectus in electronic format may be made available on websites maintained by one or more of the underwriters or their respective affiliates. The representatives may agree with us to allocate a number of shares of our common stock to underwriters for sale to their online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters' or their respective affiliates' websites and any information contained in any other website maintained by any of the underwriters or their respective affiliates is not part of this prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors in this offering.

**Other Relationships**

The underwriters are full-service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, principal investment, hedging, financing and brokerage activities. The underwriters and their respective affiliates may, from time to time, engage in transactions with and perform services for us in the ordinary course of their business for which they may receive customary fees and reimbursement of expenses. In the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (which may include bank loans or credit default swaps) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long or short positions in such securities and instruments.

**Notice to Prospective Investors in the European Economic Area**

In relation to each member state of the European Economic Area that has implemented the Prospectus Directive (each, a relevant member state), with effect from and including the date on which the Prospectus Directive is implemented in that relevant member state (the relevant implementation date), an offer of shares of our common stock described in this prospectus may not be made to the public in that relevant member state other than:

- to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- to fewer than 100 or, if the relevant member state has implemented the relevant provision of the 2010 PD Amending Directive, 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the relevant Dealer or Dealers nominated by us for any such offer; or
- in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares of our common stock shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive.

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

The sellers of the shares of our common stock have not authorized and do not authorize the making of any offer of shares of our common stock through any financial intermediary on their behalf, other than offers made by the underwriters with a view to the final placement of the shares of our common stock as contemplated in this prospectus. Accordingly, no purchaser of the shares of our common stock, other than the underwriters, is authorized to make any further offer of the shares of our common stock on behalf of the sellers or the underwriters.

**Notice to Prospective Investors in the United Kingdom**

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (1) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, or the Order, or (2) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (each such person being referred to as a relevant person).

This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

**Notice to Prospective Investors in Australia**

No prospectus or other disclosure document (as defined in the Corporations Act 2001 (Cth) of Australia, or Corporations Act) in relation to our common stock has been or will be lodged with the Australian Securities & Investments Commission, or ASIC. This document has not been lodged with ASIC and is only directed to certain categories of exempt persons. Accordingly, if you receive this document in Australia:

- you confirm and warrant that you are either:
    - a "sophisticated investor" under Section 708(8)(a) or (b) of the Corporations Act;
    - a "sophisticated investor" under Section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to us which complies with the requirements of Section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made; a person associated with the company under Section 708(12) of the Corporations Act; or
    - a "professional investor" within the meaning of Section 708(11)(a) or (b) of the Corporations Act, and to the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act any offer made to you under this document is void and incapable of acceptance; and
- you warrant and agree that you will not offer any of our common stock for resale in Australia within 12 months of that common stock being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under Section 708 of the Corporations Act.

**Notice to Prospective Investors in Canada**

The securities may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the securities must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

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

Pursuant to Section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

**Notice to Prospective Investors in Chile**

The shares of our common stock are not registered in the Securities Registry (Registro de Valores) or subject to the control of the Chilean Securities and Exchange Commission (Superintendencia de Valores y Seguros de Chile). This prospectus and other offering materials relating to the offer of the shares do not constitute a public offer of, or an invitation to subscribe for or purchase, the shares in the Republic of Chile, other than to individually identified purchasers pursuant to a private offering within the meaning of Article 4 of the Chilean Securities Market Act (Ley de Mercado de Valores) (an offer that is not "addressed to the public at large or to a certain sector or specific group of the public").

**Notice to Prospective Investors in France**

Neither this prospectus nor any other offering material relating to the shares of our common stock described in this prospectus has been submitted to the clearance procedures of the *Autorité des Marchés Financiers* or of the competent authority of another member state of the European Economic Area and notified to the *Autorité des Marchés Financiers*. The shares of our common stock have not been offered or sold and will not be offered or sold, directly or indirectly, to the public in France. Neither this prospectus nor any other offering material relating to the shares of our common stock has been or will be:

- released, issued, distributed or caused to be released, issued or distributed to the public in France; or
- used in connection with any offer for subscription or sale of the shares of our common stock to the public in France.

Such offers, sales and distributions will be made in France only:

- to qualified investors (*investisseurs qualifiés*) and/or to a restricted circle of investors (*cercle restreint d'investisseurs*), in each case investing for their own account, all as defined in and in accordance with articles L.411-2, D.411-1, D.411-2, D.734-1, D.744-1, D.754-1and D.764-1 of the French Code monétaire et financier;

- to investment services providers authorized to engage in portfolio management on behalf of third parties; or

- in a transaction that, in accordance with article L.411-2-II-1° -or-2° -or 3° of the French Code *monétaire et financier* and article 211-2 of the General Regulations (*Règlement Général*) of the *Autorité des Marchés Financiers*, does not constitute a public offer (*appel public à l'épargne*).

The shares of our common stock may be resold directly or indirectly, only in compliance with articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French Code *monétaire et financier*.

**Notice to Prospective Investors in Hong Kong**

The shares of our common stock may not be offered or sold in Hong Kong by means of any document other than (1) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), or (2) to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder, or (3) in other circumstances which do not result in the document being a "prospectus" within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong) and no advertisement, invitation or document relating to the shares of our common stock may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares of our common stock which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

**Notice to Prospective Investors in the State of Israel**

In the State of Israel this prospectus shall not be regarded as an offer to the public to purchase shares of common stock under the Israeli Securities Law, 5728 - 1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728 - 1968, including, inter alia, if: (1) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions, or the Addressed Investors; or (2) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728 - 1968, subject to certain conditions, or Qualified Investors. The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. We have not and will not take any action that would require us to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728 - 1968. We have not and will not distribute this prospectus or make, distribute or direct an offer to subscribe for our common stock to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728 - 1968. In particular, we may request that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (1) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728 - 1968; (2) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728 - 1968 regarding Qualified Investors is applicable to it; (3) that it will abide by all provisions set forth in the Israeli Securities Law, 5728 - 1968 and the regulations promulgated thereunder in connection with this offering; (4) that the shares of common stock that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728 - 1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728 -1968; and (5) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor's name, address and passport number or Israeli identification number.

**Notice to Prospective Investors in Japan**

The shares of our common stock offered in this prospectus have not been and will not be registered under the Financial Instruments and Exchange Law of Japan. The shares of our common stock have not been offered or sold and will not be offered or sold, directly or indirectly, in Japan or to or for the account of any resident of Japan (including any corporation or other entity organized under the laws of Japan), except (1) pursuant to an exemption from the registration requirements of the Financial Instruments and Exchange Law and (2) in compliance with any other applicable requirements of Japanese law.

**Notice to Prospective Investors in Singapore**

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares of our common stock may not be circulated or distributed, nor may the shares of our common stock be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (1) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (2) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA or (3) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to compliance with conditions set forth in the SFA.

Where the shares of our common stock are subscribed or purchased under Section 275 of the SFA by a relevant party which is:

- a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

- a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, shares, debentures and units of shares of our common stock and debentures of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares of our common stock pursuant to an offer made under Section 275 of the SFA except:

    - to an institutional investor (for corporations, under Section 274 of the SFA) or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares of our common stock and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than $200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions specified in Section 275 of the SFA;

    - where no consideration is or will be given for the transfer; or

    - where the transfer is by operation of law.

## LEGAL MATTERS

The validity of the shares of common stock being offered by this prospectus will be passed upon for us by Cooley LLP, Reston, Virginia. Goodwin Procter LLP, New York, New York, is representing the underwriters in connection with this offering.

## EXPERTS

The financial statements of PhaseBio Pharmaceuticals, Inc. as of December 31, 2016 and 2017, and for the years then ended, have been included herein and in the registration statement in reliance upon the report of KPMG LLP, independent registered public accounting firm, appearing elsewhere herein, and upon the authority of said firm as experts in accounting and auditing. The audit report covering the December 31, 2017 financial statements contains an explanatory paragraph that states we have incurred recurring losses and negative cash flows from operations that raise substantial doubt about our ability to continue as a going concern. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

## WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act, with respect to the shares of common stock being offered by this prospectus, which constitutes a part of the registration statement. This prospectus does not contain all of the information in the registration statement and its exhibits. For further information with respect to us and the common stock offered by this prospectus, we refer you to the registration statement and its exhibits. Statements contained in this prospectus as to the contents of any contract or any other document referred to are not necessarily complete, and in each instance, we refer you to the copy of the contract or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference.

You can read our SEC filings, including the registration statement, over the internet at the SEC's website at www.sec.gov. You may also read and copy any document we file with the SEC at its public reference facilities at 100 F Street, N.E., Washington, D.C. 20549. You may also obtain copies of these documents at prescribed rates by writing to the Public Reference Section of the SEC at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference facilities.

Upon completion of this offering, we will be subject to the information reporting requirements of the Exchange Act, and we will file reports, proxy statements and other information with the SEC. These reports, proxy statements and other information will be available for inspection and copying at the public reference room and web site of the SEC referred to above. We also maintain a website at www.phasebio.com, at which you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. However, the information contained in or accessible through our website is not part of this prospectus or the registration statement of which this prospectus forms a part.

**PhaseBio Pharmaceuticals, Inc.**

**Index to Financial Statements**

## Report of Independent Registered Public Accounting Firm

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

*Opinion on the Financial Statements*

We have audited the accompanying balance sheets of PhaseBio Pharmaceuticals, Inc. (the Company) as of December 31, 2016 and 2017, the related statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders' deficit, and cash flows for the years then ended, and the related notes (collectively, the financial statements). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2016 and 2017, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

*Going Concern*

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has incurred recurring losses and negative cash flows from operations that raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

*Basis for Opinion*

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ KPMG LLP

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

Philadelphia, Pennsylvania
July 27, 2018, except for the recapitalization described in Note 2, as to which the date is October 5, 2018.

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

| | December 31, 2016 | December 31, 2017 | June 30, 2018 | Pro Forma June 30, 2018 |
|---|---|---|---|---|
| | | | (unaudited) | |
| **Assets** | | | | |
| Current assets: | | | | |
| Cash and cash equivalents | $ 3,715 | $ 13,406 | $ 8,734 | $ 28,446 |
| Prepaid expenses and other assets | 169 | 340 | 218 | 218 |
| Total current assets | 3,884 | 13,746 | 8,952 | 28,664 |
| Property and equipment, net | 182 | 302 | 276 | 276 |
| Deferred offering costs | — | — | 610 | 610 |
| Other assets | 51 | 51 | 51 | 51 |
| Total assets | $ 4,117 | $ 14,099 | $ 9,889 | $ 29,601 |
| **Liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)** | | | | |
| Current liabilities: | | | | |
| Convertible promissory notes, net of discount | $ — | $ 12,095 | $ 14,140 | $ — |
| Derivative liability | — | 3,028 | 3,345 | — |
| Current portion of long-term debt | — | 761 | 2,860 | 3,360 |
| Accounts payable | 433 | 430 | 569 | 569 |
| Accrued expenses | 411 | 1,281 | 2,386 | 1,188 |
| Total current liabilities | 844 | 17,595 | 23,300 | 5,117 |
| Preferred stock warrant liability | 880 | 1,656 | 2,652 | — |
| Deferred rent | 8 | 5 | — | |
| Long-term debt | — | 2,625 | 2,630 | 4,130 |
| Total liabilities | 1,732 | 21,881 | 28,582 | 9,247 |
| Commitments *(Note 7)* | | | | |
| Redeemable convertible preferred stock, $0.001 par value; 18,292,703 shares authorized; 9,131,999 shares issued and outstanding at December 31, 2016 and 2017, and June 30, 2018; liquidation preference of $89,776,055 at December 31, 2017 and June 30, 2018; no shares authorized, issued and outstanding, proforma | 89,567 | 89,634 | 89,667 | — |
| Stockholders' equity (deficit): | | | | |
| Common stock, $0.001 par value; 20,789,273 shares authorized; 773,208 shares issued and 743,241 shares outstanding at December 31, 2016; 775,755 shares issued and 745,788 shares outstanding at December 31, 2017 and June 30, 2018; 14,588,404 shares outstanding, pro forma | 1 | 1 | 1 | 15 |
| Treasury stock, at cost, 29,967 shares as of December 31, 2016 and 2017 and June 30, 2018 | (24) | (24) | (24) | (24) |
| Additional paid-in capital | 1,659 | 1,672 | 1,805 | 130,505 |
| Accumulated deficit | (88,818) | (99,065) | (110,142) | (110,142) |
| Total stockholders' equity (deficit) | (87,182) | (97,416) | (108,360) | 20,354 |
| Total liabilities, redeemable convertible preferred stock, and stockholders' equity (deficit) | $ 4,117 | $ 14,099 | $ 9,889 | $ 29,601 |

*See accompanying notes to financial statements.*

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

| | Year Ended December 31, | | Six Months Ended June 30, | |
|---|---|---|---|---|
| | 2016 | 2017 | 2017 | 2018 |
| | | | (unaudited) | |
| Operating expenses: | | | | |
| Research and development | $ 7,376 | $ 6,210 | $ 3,057 | $ 5,425 |
| General and administrative | 2,125 | 2,328 | 1,135 | 1,560 |
| Total operating expenses | 9,501 | 8,538 | 4,192 | 6,985 |
| Loss from operations | (9,501) | (8,538) | (4,192) | (6,985) |
| Other income (expense): | | | | |
| Interest income | 29 | 52 | 15 | 72 |
| Interest expense | — | (2,723) | (987) | (2,851) |
| Change in fair value of warrant liability | 252 | 1,019 | 125 | (996) |
| Change in fair value of derivative liability | — | (57) | (113) | (317) |
| Total other income (expense) | 281 | (1,709) | (960) | (4,092) |
| Net loss | $ (9,220) | $ (10,247) | $ (5,152) | $ (11,077) |
| Net loss per common share, basic and diluted | $ (12.41) | $ (13.78) | $ (6.93) | $ (14.85) |
| Weighted average common shares outstanding, basic and diluted | 742,808 | 743,470 | 743,241 | 745,788 |
| Pro forma net loss per common share, basic and diluted (unaudited) | | $ (0.76) | | $ (0.58) |
| Pro forma weighted average common shares outstanding, basic and diluted (unaudited) | | 11,235,815 | | 12,376,871 |
| Comprehensive loss: | | | | |
| Net loss | $ (9,220) | $ (10,247) | $ (5,152) | $ (11,077) |
| Net unrealized gain on short-term investments | 6 | — | — | — |
| Comprehensive loss | $ (9,214) | $ (10,247) | $ (5,152) | $ (11,077) |

*See accompanying notes to financial statements.*

## PHASEBIO PHARMACEUTICALS, INC.
## Statements of Redeemable Convertible Preferred Stock and Stockholders' Deficit
## (in thousands, except share amounts)

| | Redeemable Convertible Preferred Stock | | Stockholders' Equity (Deficit) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Common Stock | | Treasury Stock | | Additional Paid-in Capital | Accumulated Deficit | Accumulated Other Comprehensive Income (Loss) | Total Stockholders' Deficit |
| | Shares | Amount | Shares | Amount | Shares | Amount | | | | |
| **Balance at December 31, 2015** | 9,131,999 | $ 89,500 | 772,305 | $ 1 | (29,967) | $ (24) | $ 1,565 | $ (79,598) | $ (6) | $ (78,062) |
| Exercise of stock options | — | — | 903 | — | — | — | 1 | — | — | 1 |
| Stock-based compensation | — | — | — | — | — | — | 160 | — | — | 160 |
| Accretion of redeemable preferred stock to redemption value | — | 67 | — | — | — | — | (67) | — | — | (67) |
| Unrealized gain on short-term investments | — | — | — | — | — | — | — | — | 6 | 6 |
| Net loss | — | — | — | — | — | — | — | (9,220) | — | (9,220) |
| **Balance at December 31, 2016** | 9,131,999 | 89,567 | 773,208 | 1 | (29,967) | (24) | 1,659 | (88,818) | — | (87,182) |
| Exercise of stock options | — | — | 2,547 | — | — | — | 3 | — | — | 3 |
| Stock-based compensation | — | — | — | — | — | — | 77 | — | — | 77 |
| Accretion of redeemable preferred stock to redemption value | — | 67 | — | — | — | — | (67) | — | — | (67) |
| Net loss | — | — | — | — | — | — | — | (10,247) | — | (10,247) |
| **Balance at December 31, 2017** | 9,131,999 | 89,634 | 775,755 | 1 | (29,967) | (24) | 1,672 | (99,065) | — | (97,416) |
| Stock-based compensation (unaudited) | — | — | — | — | — | — | 166 | — | — | 166 |
| Accretion of redeemable preferred stock to redemption value (unaudited) | — | 33 | — | — | — | — | (33) | — | — | (33) |
| Net loss (unaudited) | — | — | — | — | — | — | — | (11,077) | — | (11,077) |
| **Balance at June 30, 2018 (unaudited)** | 9,131,999 | $ 89,667 | 775,755 | $ 1 | (29,967) | $ (24) | $ 1,805 | $ (110,142) | $ — | $ (108,360) |

*See accompanying notes to financial statements.*

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

| | Year Ended December 31, | | Six Months Ended June 30, | |
|---|---|---|---|---|
| | 2016 | 2017 | 2017 | 2018 |
| | | | (unaudited) | |
| **Operating activities** | | | | |
| Net loss | $ (9,220) | $ (10,247) | $ (5,152) | $ (11,077) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | | | |
| Depreciation and amortization | 92 | 96 | 40 | 54 |
| Stock-based compensation | 160 | 77 | 38 | 166 |
| Non-cash interest expense | — | 2,711 | 987 | 2,761 |
| Change in fair value warrant liability | (252) | (1,019) | (125) | 996 |
| Change in fair value derivative liability | — | 57 | 113 | 317 |
| Changes in operating assets and liabilities: | | | | |
| Prepaid expenses and other assets | 32 | 40 | 30 | 115 |
| Accounts payable | (344) | (213) | 57 | (115) |
| Accrued expenses | (161) | 242 | 267 | 149 |
| Deferred rent | 5 | (3) | — | (5) |
| Net cash used in operating activities | (9,688) | (8,259) | (3,745) | (6,639) |
| **Investing activities** | | | | |
| Lease deposit | (8) | — | — | — |
| Purchase of short-term investments | (1,599) | — | — | — |
| Proceeds from sale of short-term investments | 10,950 | — | — | — |
| Purchases of property and equipment | (94) | (216) | (67) | (28) |
| Net cash provided by (used in) investing activities | 9,249 | (216) | (67) | (28) |
| **Financing activities** | | | | |
| Proceeds from convertible promissory notes | — | 14,683 | 6,601 | — |
| Proceeds from term loan | — | 3,480 | — | 1,995 |
| Proceeds from exercise of stock options | 1 | 3 | — | — |
| Net cash provided by financing activities | 1 | 18,166 | 6,601 | 1,995 |
| Net (decrease) increase in cash and cash equivalents | (438) | 9,691 | 2,789 | (4,672) |
| Cash and cash equivalents at the beginning of the period | 4,153 | 3,715 | 3,715 | 13,406 |
| Cash and cash equivalents at the end of the period | $ 3,715 | $ 13,406 | $ 6,504 | $ 8,734 |
| **Supplemental disclosure for cash flow** | | | | |
| Cash paid for interest | $ — | $ 12 | $ — | $ 90 |
| **Supplemental disclosure of cash flow information** | | | | |
| Accretion of redeemable convertible preferred stock | $ 67 | $ 67 | $ 33 | $ 33 |
| Issuance of warrants in conjunction with debt | $ — | $ 1,795 | $ 1,046 | $ — |
| Issuance of derivative in conjunction with debt | $ — | $ 2,971 | $ 1,309 | $ — |
| Purchases of property and equipment included in accounts payable | $ — | $ — | $ 135 | $ — |
| Deferred offering costs included in accounts payable and accrued expenses | $ — | $ — | $ — | $ 604 |

*See accompanying notes to financial statements.*

**PHASEBIO PHARMACEUTICALS INC.**

**Notes to the Financial Statements**
**(information as of June 30, 2018 and for the six months ended June 30, 2017 and 2018 is unaudited)**

## 1. Organization and 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 we are developing for the treatment of patients on ticagrelor who are experiencing a major bleeding event or those who require urgent surgery. The Company recently completed a Phase 1 clinical trial of PB2452 in healthy subjects. 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, or ELP, technology, which also serves as the engine for future product pipeline candidates.

### Liquidity

The Company has experienced net losses and negative cash flows from operations since its inception and, as of June 30, 2018, had an accumulated deficit of $110.1 million. The Company expects to continue to incur net losses for at least the next several years. As of June 30, 2018, the Company had cash and cash equivalents of $8.7 million and working capital deficit of $14.3 million. The Company will require additional cash funding to continue to execute its strategic plan and fund operations beyond December 31, 2018. These factors raise substantial doubt about the Company's ability to continue as a going concern. The accompanying financial statements have been prepared assuming the Company will continue as a going concern. This basis of accounting contemplates the recovery of the Company's assets and the satisfaction of liabilities in the normal course of business and does not include any adjustments to reflect the possible future effects of the recoverability and classification of assets or the amounts and classification of liabilities that might be necessary should the Company be unable to continue as a going concern.

The Company will seek to obtain additional capital through the sale of debt or equity financings or other arrangements to fund operations; however, there can be no assurance that the Company will be able to raise needed capital under acceptable terms, if at all. The sale of additional equity may dilute existing stockholders and newly issued shares may contain senior rights and preferences compared to currently outstanding shares of common stock. Issued debt securities may contain covenants and limit the Company's ability to pay dividends or make other distributions to stockholders. If the Company is unable to obtain such additional financing, future operations would need to be scaled back or discontinued.

### Unaudited Interim Liquidity Position

In August 2018, the Company received $17.7 million in net proceeds from the sale of Series D redeemable convertible preferred stock. Additionally, in August 2018, the Company borrowed $2.0 million under its term loan with Silicon Valley Bank. As a result of these financing activities, management believes the Company has sufficient capital to execute its strategic plan and fund operations through the third quarter of 2019.

## 2. Basis of Presentation and Significant Accounting Policies

*Basis of Presentation*

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

*Use of Estimates*

The preparation of the Company's financial statements requires management to make estimates and assumptions that impact the reported amounts of assets, liabilities and expenses and the disclosure of contingent assets and liabilities in the Company's financial statements and accompanying notes. The most significant estimates in the Company's financial statements relate to the valuation of redeemable convertible preferred stock warrants, equity awards 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 may ultimately materially differ from these estimates and assumptions.

*Unaudited Interim Financial Information*

The accompanying balance sheet as of June 30, 2018, statements of operations and comprehensive loss and cash flows for the six months ended June 30, 2017 and 2018 and the statements of redeemable convertible preferred stock and stockholders' deficit for the six months ended June 30, 2018 and related notes are unaudited. The unaudited financial statements have been prepared on a basis consistent with the audited financial statements and, in the opinion of management, reflect all adjustments (consisting of normal recurring adjustments) considered necessary to state fairly the Company's financial position as of June 30, 2018 and the results of its operations and cash flows for the six months ended June 30, 2017 and 2018. The results for the six months ended June 30, 2018 are not necessarily indicative of the results to be expected for the year ending December 31, 2018 or for any other interim period.

*Unaudited Pro Forma Information*

The unaudited pro forma balance sheet as of June 30, 2018 gives effect to:

- the automatic conversion of all outstanding shares of the Company's redeemable convertible preferred stock, including the conversion of 3,923,168 shares of Series D redeemable convertible preferred stock issued in August 2018, into an aggregate of 13,064,781 shares of common stock, based on an assumed initial public offering price of $13.00 per share, the midpoint of the price range set forth on the cover page of this prospectus;

- the exercise of outstanding warrants to purchase 777,835 shares of the Company's redeemable convertible preferred stock, including warrants to purchase 368,582 shares of Series C-1 redeemable convertible preferred stock issued in August 2018, and the automatic conversion thereof into 777,835 shares of common stock, which the Company expects, will occur immediately prior to the closing of this offering;

- the receipt of $17.7 million in net proceeds from the sale of Series D redeemable convertible preferred stock in August 2018;

- the conversion of the Company's outstanding convertible promissory notes, and accrued interest thereon; and

- the receipt of $2.0 million in additional borrowings under the Company's loan and security agreement with Silicon Valley Bank.

The unaudited pro forma balance sheet assumes that the completion of the proposed initial public offering (the "IPO") had occurred as of June 30, 2018 and excludes shares of common stock issued in the IPO and any related net proceeds.

*Recapitalization*

The Company effected a 11.0634-for-1 reverse split of its common stock and redeemable convertible preferred stock on October 4, 2018. The reverse split combined each approximately 11 shares of the Company's issued and outstanding common stock and redeemable convertible preferred stock into one share of common stock or redeemable convertible preferred stock, as applicable. No fractional shares were issued in connection with the reverse split. Any fractional share resulting from the reverse split was rounded down to the nearest whole share, and in lieu of any fractional shares, the Company will pay in cash to the holders of such fractional shares an amount equal to the fair value, as determined by the board of directors, of such fractional shares. All share, per share and related information presented in the financial statements and accompanying notes have been retroactively adjusted, where applicable, to reflect the reverse stock split.

*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 deposits in federally insured financial institutions in excess of federally insured limits. The Company has not experienced any losses in such accounts and believes it is not exposed to significant risk on its cash and cash equivalents.

*Cash and Cash Equivalents*

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

*Restricted Cash*

The Company had restricted cash of $20,000 as of December 31, 2016, December 31, 2017 and June 30, 2018, which was held in a certificate of deposit at the Company's bank to secure the Company's corporate credit card. Restricted cash is included in the other assets account on the accompanying balance sheets.

*Fair Value of Financial Instruments*

The carrying amounts of prepaid expenses and other current assets, accounts payable and accrued expenses are reasonable estimates of their fair value because of the short maturity of these items. The carrying amount of the convertible promissory notes approximates fair value because the interest rates on these instruments are reflective of rates that the Company could obtain on unaffiliated third party debt with similar terms and conditions. Based on the borrowing rates currently available to the Company for loans with similar terms, the Company believes the fair value of the term loan approximates its carrying value (see Note 6).

*Property and Equipment*

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

*Long-Lived Assets*

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

*Preferred Stock Warrant Liability*

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

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

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

*Research and Development Expenses*

Research and development costs are expensed as incurred.

*Stock-Based Compensation*

Stock-based compensation expense represents the grant date fair value of employee stock option grants recognized over the requisite service period of the awards on a straight-line basis. Stock option awards to non-employees are subject to periodic revaluation over their vesting terms.

*Income Taxes*

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

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

*Grant Revenue*

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

*Net Loss Per Share*

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

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

| | Year Ended December 31, | | Six Months Ended June 30, | |
|---|---|---|---|---|
| | 2016 | 2017 | 2017 | 2018 |
| | | | (unaudited) | |
| Redeemable convertible preferred stock | 9,131,999 | 9,131,999 | 9,131,999 | 9,131,999 |
| Common stock options | 1,001,546 | 1,075,209 | 1,084,243 | 1,210,776 |
| Warrants to purchase redeemable convertible preferred stock | 132,246 | 486,356 | 269,225 | 484,850 |
| Total | 10,265,791 | 10,693,564 | 10,485,467 | 10,827,625 |

*Unaudited Pro Forma Net Loss Per Share*

The following table summarizes the unaudited pro forma net loss per common share (in thousands, except share and per share amounts):

| | Year Ended December 31, 2017 | Six Months Ended June 30, 2018 |
|---|---|---|
| | | (unaudited) |
| **Numerator** | | |
| Net loss | $ (10,247) | $ (11,077) |
| Add: | | |
| Interest expense on convertible promissory notes | 2,662 | 2,629 |
| Change in fair value of derivative liability | 57 | 317 |
| Change in fair value of preferred stock warrant liability | (1,019) | 996 |
| Pro forma net loss | $ (8,547) | $ (7,135) |
| **Denominator** | | |
| Weighted average common shares outstanding, basic and diluted | 743,740 | 745,788 |
| Add: | | |
| Pro forma adjustments to reflect assumed conversion of convertible promissory notes | 1,086,839 | 2,080,209 |
| Pro forma adjustments to reflect assumed conversion of redeemable convertible preferred stock | 9,141,613 | 9,141,613 |
| Pro forma adjustments to reflect assumed effect of net exercise of redeemable convertible preferred stock warrants | 263,893 | 409,261 |
| Shares used to compute pro forma net loss per share, basic and diluted | 11,235,815 | 12,376,871 |
| Pro forma net loss per common share, basic and diluted | $ (0.76) | $ (0.58) |

*Recent Accounting Pronouncements*

In February 2016, the FASB issued ASU No. 2016-02, *Leases*. This update amends the current accounting guidance for lease transactions. Under the new guidance, a lessee will be required to recognize both assets and liabilities for any leases in excess of twelve months. Additionally, certain qualitative and quantitative disclosures will also be required in the financial statements. This guidance will be effective for public companies for annual and interim periods beginning after December 15, 2018. For all other entities, including emerging growth companies if a one-time deferral is elected, this standard is effective for annual reporting periods beginning after December 15, 2019, and interim periods within annual periods beginning after December 15, 2020. Early adoption is permitted. The Company is in the process of determining the impact of the adoption of this update will have on its financial statements.

In August 2016, the FASB issued ASU No. 2016-15, *Classification of Certain Cash Receipts and Cash Payments (Topic 230)*. ASU 2016-15 addresses eight specific cash flow issues with the objective of reducing the existing diversity in practice for certain cash receipts and cash payments. The standard is effective for annual

reporting periods beginning after December 15, 2018 and interim periods reporting within fiscal years beginning after December 15, 2019, with early adoption permitted. The Company does not believe the adoption of this guidance will have a material impact on its financial statements.

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

## 3. Fair Value Measurement

ASC 820, *Fair Value Measurement*, provides guidance on the development and disclosure of fair value measurements. Under this accounting guidance, 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 accounting guidance 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 estimates 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, using the following inputs: the risk-free interest rates; the expected dividend rates; the remaining contractual life of the warrants; and the expected volatility of the price of the underlying common stock. The estimates are based, in part, on subjective assumptions and could differ materially in the future. Changes to these assumptions as well as the fair value of the Company's stock on the reporting date can have a significant impact on the fair value of the redeemable convertible preferred stock warrant liability.

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 Using | | |
|---|---|---|---|---|
| | Total | Quoted Prices in Active Markets for Identical Assets (Level 1) | Significant Other Observable Inputs (Level 2) | Significant Unobservable Inputs (Level 3) |
| **As of December, 31, 2016:** | | | | |
| Cash equivalents | $ 2,820 | $ 2,820 | $ — | $ — |
| Preferred stock warrant liability | 880 | — | — | 880 |
| **As of December, 31, 2017:** | | | | |
| Cash equivalents | $ 12,472 | $ 12,472 | $ — | $ — |
| Preferred stock warrant liability | 1,656 | — | — | 1,656 |
| Derivative liability | 3,028 | — | — | 3,028 |
| **As of June 30, 2018 (unaudited)** | | | | |
| Cash equivalents | $ 7,544 | $ 7,544 | $ — | $ — |
| Preferred stock warrant liability | 2,652 | — | — | 2,652 |
| Derivative liability | 3,345 | — | — | 3,345 |

The following weighted-average assumptions were used in determining the fair value of the outstanding preferred stock warrant liabilities valued using the Black-Scholes option pricing model as of December 31, 2016 and 2017 and June 30, 2018:

| | December 31, | | June 30, |
|---|---|---|---|
| | 2016 | 2017 | 2018 |
| | | | (unaudited) |
| Expected volatility | 67.3% | 68.0% | 67.3% |
| Risk-free interest rate | 1.7% | 2.2% | 2.7% |
| Contractual term (in years) | 4.09 | 5.89 | 5.41 |
| Expected dividend yield | — | — | — |

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

| | December 31, | | June 30, |
|---|---|---|---|
| | 2016 | 2017 | 2018 |
| | | | (unaudited) |
| Series AA | $ 9.85 | $ 5.75 | $ — |
| Series B | $ 7.74 | $ 3.76 | $ 5.97 |
| Series C-1 | $ — | $ 3.76 | $ 5.97 |

The following tables present activity for the redeemable preferred stock warrant liability and the derivative liability measured at fair value using significant unobservable Level 3 inputs as of December 31, 2016 and 2017 and June 30, 2018 (in thousands):

| | Preferred Stock Warrant Liability |
|---|---|
| Balance at January 1, 2016 | $ 1,132 |
| Changes in fair value reflected as change in fair value of warrant liability | (252) |
| Balance at December 31, 2016 | 880 |
| Issuance of warrants | 1,795 |
| Changes in fair value reflected as change in fair value of warrant liability | (1,019) |
| Balance at December 31, 2017 | 1,656 |
| Changes in fair value reflected as change in fair value of warrant liability (unaudited) | 996 |
| Balance at June 30, 2018 (unaudited) | $ 2,652 |

| | |
|---|---|
| Balance at December 31, 2016 | $ — |
| Issuance of derivative | 2,971 |
| Changes in fair value reflected as change in fair value of derivative liability | 57 |
| Balance at December 31, 2017 | 3,028 |
| Changes in fair value reflected as change in fair value of derivative liability (unaudited) | 317 |
| Balance at June 30, 2018 (unaudited) | $ 3,345 |

## 4. Property and Equipment

Property and equipment consists of the following (in thousands):

| | As of December 31, | | As of June 30, |
|---|---|---|---|
| | 2016 | 2017 | 2018 |
| | | | (unaudited) |
| Lab equipment | $ 1,483 | $ 1,681 | $ 1,684 |
| Computer hardware, software and telephone | 159 | 174 | 199 |
| Furniture and fixtures | 67 | 70 | 70 |
| Leasehold improvements | 22 | 22 | 22 |
| | 1,731 | 1,947 | 1,975 |
| Less accumulated depreciation | (1,549) | (1,645) | (1,699) |
| Property and equipment, net | $ 182 | $ 302 | $ 276 |

## 5. Accrued Expenses

Accrued expenses consist of the following (in thousands):

| | As of December 31, | | As of June 30, |
|---|---|---|---|
| | 2016 | 2017 | 2018 |
| | | | (unaudited) |
| Payroll and related costs | $ 190 | $ 346 | $ 202 |
| Research and development expenses | 181 | 197 | 101 |
| Professional fees and other services | 40 | 100 | 850 |
| Interest payable | — | 628 | 1,233 |
| Other | — | 10 | — |
| Accrued expenses | $ 411 | $ 1,281 | $ 2,386 |

## 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 bear interest at the rate of 8%. 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. In the event that the equity financing is less than $10.0 million, or does not occur prior to the stated maturity date, the 2017 Notes, upon written consent of the Company's board of directors, its largest stockholder and holders of a majority of the principal amount of the then-outstanding 2017 Notes, can either (a) convert the principal plus accrued interest on the 2017 Notes into shares of the stock issued in such financing at a price equal to 80% of the lowest issue price, or (b) convert the principal amount plus accrued interest into shares of Series C-1 at $9.659 per share, or (c) the 2017 Notes become immediately due and payable.

The 2017 Notes can convert 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 is 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.

The 2017 Notes have a stated maturity date of March 31, 2018. In October 2017, the noteholders entered into a subordination agreement with Silicon Valley Bank. Under the terms of the subordination agreement, the noteholders will not demand or receive any payment on the 2017 Notes until all amounts owed under the Loan and Security Agreement with Silicon Valley Bank are repaid in full on June 1, 2020.

In connection with the 2017 Notes, the Company issued warrants to the noteholders to purchase 304,397 shares of Series C-1. The warrants are exercisable for $0.12 per share and 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. 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 is being amortized to interest expense over the term of the 2017 Notes using the effective-interest method.

Interest expense, including the debt discount related to the 2017 Notes, were $2.7 million, $1.0 million, and $2.6 million for the year ended December 31, 2017 and the six months ended June 30, 2017 and 2018, respectively.

*Term Loan*

In October 2017, the Company entered into a Loan and Security Agreement ("SVB Loan") with Silicon Valley Bank ("SVB"), pursuant to which the Company may 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 become available upon the achievement of certain clinical and regulatory milestones. Under 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 is 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 has the option to prepay all, but not less than all, of the borrowed amounts, provided that the Company will be obligated to pay a prepayment fee equal to (a) 3.0% of the outstanding principal balance of the applicable Growth Capital Advances if prepayment is 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 is 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 is 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 will be extended to December 31, 2018 if the Company borrows Tranche B and Tranche C. Additionally, all Capital Growth Advances will mature on June 1, 2020; however, if the Company draws Tranche B and Tranche C, the maturity date will be December 31, 2020. On April 30, 2018, the Company borrowed $2.0 million under Tranche B.

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

The Company recorded a debt discount of $0.4 million for the estimated fair value of warrants and debt issuance costs upon the borrowing of Tranche A and Tranche B, which is being amortized to interest expense over the term of the SVB Loan using the effective-interest method. As of December 31, 2017, and June 30, 2018, the Company had $3.5 million and $5.5 million, respectively, of outstanding principal under the SVB Loan and $3.4 million and $5.5 million, respectively, is reflected on the balance sheet net of debt discounts. Interest expense, including amortization of debt discount related to the term debt, totaled $0.1 million for the year ended December 31, 2017 and $0.2 million for the six months ended June 30, 2018. The Company is in compliance with all covenants under the SVB Loan as of December 31, 2017.

The future principal payments for the Company's Growth Capital Advances as of December 31, 2017 are as follows (in thousands):

| Year Ending December 31, | |
|---|---|
| 2018 | $ 875 |
| 2019 | 1,750 |
| 2020 | 875 |
| | $ 3,500 |

## 7. Commitments

### *Facilities Lease*

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 originally to expire on July 31, 2015. In December 2014, the Malvern Lease was amended to extend its term to July 31, 2018. In February 2018, the Malvern lease was further amended to extend its term to September 30, 2023.

At December 31, 2017, the Company's future minimum commitments under its non-cancelable operating leases were as follows (in thousands):

| Year Ending December 31, | |
|---|---|
| 2018 | $ 262 |
| 2019 | 251 |
| 2020 | 256 |
| 2021 | 262 |
| 2022 | 267 |
| Thereafter | 203 |
| Total | $ 1,501 |

Rent expense was $0.4 million for each of the years ended December 31, 2016 and 2017, and $0.2 million for each of the six months ended June 30, 2017 and 2018.

## 8. Preferred Stock Warrants

The Company accounts for its warrants to purchase shares of redeemable convertible preferred stock issued as liabilities as they are exercisable for a redeemable instrument. The Company will continue to adjust the liability for changes in fair value of these warrants until the earlier of: (1) exercise of warrants; (2) expiration of warrants; (3) a change of control of the Company; or (4) the consummation of the Company's IPO, at which time the liability will be reclassified to stockholders' equity.

The following table summarizes the outstanding redeemable convertible preferred stock warrants and the corresponding exercise price as of December 31, 2016 and 2017 and June 30, 2018:

| | Number of Shares Outstanding | | | | |
|---|---|---|---|---|---|
| | December 31, | | June 30, | Exercise | Expiration |
| | 2016 | 2017 | 2018 | Price | Date |
| | | | (unaudited) | | |
| Series AA warrants | 1,506 | 1,506 | — | $ 13.28 | March 7, 2018 |
| 2009 Series B warrants | 25,884 | 25,884 | 25,884 | 9.659 | December 22, 2019 |
| 2014 Series B warrants | 104,856 | 104,856 | 104,856 | 0.12 | May 14, 2021 |
| Convertible debt Series C-1 warrants | — | 304,397 | 304,397 | 0.12 | January 17, 2024 |
| Term loan Series C-1 warrants | — | 49,713 | 49,713 | 9.659 | October 18, 2027 |
| | 132,246 | 486,356 | 484,850 | | |

## 9. Redeemable Convertible Preferred Stock and Stockholders' Deficit

*Preferred Stock*

The Company has issued and outstanding Series 1 redeemable convertible preferred stock ("Series 1"), Series 2 redeemable preferred stock ("Series 2"), Series AA redeemable convertible preferred stock ("Series AA"), Series B redeemable convertible preferred stock ("Series B"), Series C-1, Series C-2 redeemable convertible preferred stock ("Series C-2") and Series C-3 redeemable convertible preferred stock ("Series C-3" and, collectively, "Preferred Stock").

As of December 31, 2017, the authorized, issued, and outstanding shares of preferred stock and their carrying amounts and liquidation values were as follows (in thousands, except share amounts):

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

As of June 30, 2018, the authorized, issued, and outstanding shares of redeemable preferred stock and their carrying amounts and liquidation values were as follows (in thousands, except share amounts):

| | Shares Authorized | Shares Issued and Outstanding | Carrying Amount | Liquidation Value |
|---|---|---|---|---|
| Series 1 | 132,255 | 132,255 | $ 523,314 | $ 526,778 |
| Series 2 | 1 | 1 | 242,508 | 250,000 |
| Series AA | 575,470 | 573,961 | 7,616,607 | 7,619,998 |
| Series B | 6,382,259 | 6,251,502 | 60,369,732 | 60,379,282 |
| Series C-1 | 4,524,375 | 2,174,280 | 20,914,749 | 20,999,997 |
| Series C-2 | 916,095 | — | — | — |
| Series C-3 | 790,895 | — | — | — |
| Total | 13,321,350 | 9,131,999 | $ 89,666,910 | $ 89,776,055 |

*Dividends*

The holders of the Series AA, Series B, and Series C-1 (together, the "Senior Stock") and the holders of the Series C-2 and Series C-3 (together, the "Senior Series C Stock") are entitled to receive noncumulative cash dividends, on a *pari passu* basis among the Senior Stock and the Senior Series C Stock, at the rate of 8% when and if declared by the board of directors. After payment of dividends on the Senior Series C Stock and the Senior Stock, the holders of the Series 1 are entitled to receive noncumulative dividends at the rate of 8% when and if declared by the board of directors. The holder of the Series 2 is not entitled to receive any dividends. Any declared but unpaid dividends are payable upon any liquidation, dissolution, or winding up of the Company by another entity, whether voluntary or involuntary, or conversion of the applicable shares of Preferred Stock to common stock. No dividends have been declared on the Preferred Stock.

*Liquidation Preference*

In the event of a liquidation, dissolution, or winding up of the Company, or in the event the Company merges with or is acquired by another entity, the holders of the Senior Stock and the Senior Series C Stock are entitled to be paid an amount equal to $13.28 per share of Series AA and Series C-3, $9.659 per share of Series B and Series C-1, and $11.462 per share of Series C-2, plus any declared but unpaid dividends. After payment in full of the Senior Stock and the Senior Series C Stock liquidation preference, the holder of the Series 2 is entitled to be paid a liquidation preference of $250,000. After payment in full of the Series 2 liquidation preference, the holders of the Series 1 are entitled to receive an amount equal to $3.99 per share, plus any declared but unpaid dividends. Once the preceding liquidation preferences have been paid, any remaining assets would be distributed pro rata among the holders of the Series C-1, Series C-2, Series C-3, Series B, Series AA, Series 1 and common stock.

*Voting Rights*

The holders of the Series 1, Series AA, Series B, Series C-1, Series C-2 and Series C-3 are entitled to a number of votes equal to the number of shares of common stock into which their shares can be converted. The holder of the Series 2 does not have voting rights.

*Conversion*

The shares of Series 1, Series AA, Series B, Series C-1, Series C-2 and Series C-3 are convertible into an equal number of shares of common stock, at the option of the holder, subject to certain anti-dilution adjustments. The holder of the Series 2 does not have any voluntary conversion rights. All Preferred Stock, except the Series 2, is automatically converted into common stock in the event of a firm commitment underwritten public offering of the Company's common stock with a public offering price per share of not less than $12.73 per share and aggregate net proceeds of at least $40 million (a "Qualified IPO"), or upon the agreement of 60% of the Preferred Stock, voting together as a single class on an as-converted basis. In the event of a Qualified IPO, the Series 2 will be automatically converted into shares of common stock valued at $125,000 at the initial offering price.

*Redemption*

The holders of 60% of the Preferred Stock, voting together as a single class on an as-converted basis, are entitled to require the Company to redeem all of the then-outstanding shares of Preferred Stock at any time on or after February 26, 2020. The redemption price is equal to the greater of (a) the liquidation preference, including any declared but unpaid dividends, of the applicable class of Preferred Stock or (b) the then fair market value of such Preferred Stock. If funds are insufficient to redeem all shares of Preferred Stock, all shares of Series C-1 and Senior Series C Stock will be redeemed first, then all remaining shares of Senior Stock will be redeemed, and all shares of Series 1 will be redeemed before the share of Series 2. The carrying values of the Preferred Stock are being accreted to their redemption value by a charge to additional paid-in capital, if any, then accumulated deficit. Upon election of the holders of a majority of the outstanding Series 2 and approval by the holders of at least 60% of the remaining Preferred Stock, the Company will redeem all outstanding shares of Series 2 preferred stock for an aggregate amount of $125,000.

*Common Stock Reserved for Future Issuance*

| | As of December 31, 2017 | As of June 30, 2018 |
|---|---|---|
| | | (unaudited) |
| Conversion of redeemable convertible preferred stock | 9,131,999 | 9,131,999 |
| Redeemable convertible preferred stock warrants | 486,356 | 484,850 |
| Stock options issued and outstanding | 1,075,209 | 1,210,776 |
| Authorized for future options | 45,062 | 90,256 |
| | 10,738,626 | 10,917,881 |

## 10. Stock-Based Compensation

In 2002, the Company adopted the 2002 Stock Plan (the "Plan"), which was later amended and restated, pursuant to which 90,256 shares were available for future grants as of June 30, 2018. The Plan provides for the grant of incentive stock options, nonstatutory stock options, stock awards, and stock purchase rights employees, directors, and consultants. The terms of the agreements are determined by the Company's board of directors. The Company's stock options vest based on the terms in each award agreements and generally vest over 4 years and have a term of 10 years.

The following table summarizes stock option activity for the Plan for the year ended December 31, 2017 and the six months ended June 30, 2018:

| | Total Options | Weighted-Average Exercise Price Per Share | Weighted-Average Remaining Contractual Term (in years) | Aggregate Intrinsic Value |
|---|---|---|---|---|
| Outstanding at December 31, 2016 | 1,001,546 | $ 1.62 | 8.1 | $ 58,619 |
| Granted | 99,866 | 1.44 | | |
| Exercised | (2,547) | 1.20 | | |
| Cancelled | (22,527) | 1.76 | | |
| Expired | (1,129) | 1.66 | | |
| Outstanding at December 31, 2017 | 1,075,209 | $ 1.60 | 7.3 | $ 711,328 |
| Granted (unaudited) | 135,567 | 2.26 | | |
| Outstanding at June 30, 2018 (unaudited) | 1,210,776 | $ 1.68 | 7.2 | $ 711,328 |
| Vested and expected to vest at December 31, 2017 | 987,772 | $ 1.55 | 7.2 | $ 651,900 |
| Vested and exercisable at December 31, 2017 | 643,573 | $ 1.61 | 6.7 | $ 423,738 |
| Vested and expected to vest at June 30, 2018 (unaudited) | 1,129,898 | $ 1.66 | 7.1 | $ 669,115 |
| Vested and exercisable at June 30, 2018 (unaudited) | 759,572 | $ 1.60 | 6.4 | $ 501,131 |

The weighted-average grant date fair value per share of options granted was $1.11 and $1.00 for the years ended December 31, 2016 and December 31, 2017, respectively. At December 31, 2017 and June 30, 2018, there were options outstanding to purchase 1,075,209 and 1,210,776 shares, respectively, of which 643,573 and 759,572 shares were exercisable, respectively. The aggregate intrinsic value of options exercised was $686 for the year ended December 31, 2017.

As of each of December 31 2017, and June 30, 2018, the total unrecognized compensation expense related to unvested employee and non-employee stock option awards was $0.4 million, which was expected to be recognized in expense over a weighted-average period of approximately 2.2 years and 2.5 years, respectively.

*Determining Fair Value of Stock Options*

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

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

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

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

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

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

| | Year Ended December 31, | | Six Months Ended June 30, | |
|---|---|---|---|---|
| | 2016 | 2017 | 2017 | 2018 |
| | | | (unaudited) | |
| Risk-free interest rate | 1.60% | 2.28% | 2.28% | 2.82% |
| Expected term (in years) | 7.1 | 7.1 | 7.1 | 6.1 |
| Expected volatility | 67% | 68% | 68% | 69% |
| Expected dividend yield | — | — | — | — |

Stock-based compensation expense has been reported in the Company's statements of operations and comprehensive loss for the years ended December 31, 2016 and 2017 and for the six months ended June 30, 2017 and 2018 as follows (in thousands):

| | Year Ended December 31, | | Six Months Ended June 30, | |
|---|---|---|---|---|
| | 2016 | 2017 | 2017 | 2018 |
| | | | (unaudited) | |
| General and administrative | $ 59 | $ 40 | $ 20 | $ 54 |
| Research and development | 101 | 37 | 18 | 112 |
| Total stock-based compensation | $ 160 | $ 77 | $ 38 | $ 166 |

## 11. License Agreements

*MedImmune Limited*

In November 2017, the Company entered into a license agreement ("MedImmune License") with MedImmune Limited ("MedImmune"). MedImmune is a wholly owned subsidiary of AstraZeneca plc. Pursuant to the terms of the MedImmune License, MedImmune granted the Company exclusive global rights for the purpose of developing and commercializing products under the MedImmune License ("MedImmune licensed product"). In consideration of the license and other rights granted by MedImmune, the Company made an upfront payment of $0.1 million, which was included as research and development expense for the year ended December 31, 2017. The Company is also obligated to make a series of contingent milestone payments totaling up to an aggregate of $18.0 million upon the achievement of clinical development and regulatory milestones. As of June 30, 2018, none of the clinical development or regulatory filing milestones had been met. In addition, the Company will pay MedImmune tiered royalties ranging from a mid-single-digit to low-teen percentages of net sales of any MedImmune licensed products and additional payments of up to $50.0 million in aggregate commercial milestones. The Company also must pay quarterly fees relating to technical services provided by MedImmune. The MedImmune License requires the Company to cooperate with MedImmune on commercial messaging of PB2452 and provides MedImmune with the return of rights to PB2452 if certain commercial diligence requirements are not achieved by the Company. In addition, the MedImmune License offers an option for third party product storage costs. As of December 31, 2017, the Company had incurred and reimbursed MedImmune $0.5 million for such third party product storage costs.

*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, or 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 Duke License requires the Company to apply for, prosecute and maintain United States and foreign patent rights under the Duke License. The Company incurred $0.1 million in patent legal fees for the year ended December 31, 2016. No patent expenses were incurred related to the Duke License agreement for the year ended December 31, 2017 or the six months ended June 30, 2017 or 2018.

The Company is obligated to pay up to $2.2 million upon the achievement of clinical development and regulatory milestones and up to $0.4 million upon the achievement of commercial milestones. The Duke License may be terminated by Duke if the Company fails to meet certain clinical development and regulatory milestones within specified timeframes. As of June 30, 2018, the Company was in compliance with its development obligations.

The Company is required to use commercially reasonable efforts to develop one or more products or processes and introduce them into commercial markets. Duke will receive low single-digit royalty percentages on net sales by the Company or its sublicensee, with minimum aggregate royalties of $0.2 million payable following the Company's achievement of certain commercial milestones. No sales of licensed products or services have occurred since the effective date through June 30, 2018.

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

## 12. Income Taxes

The Company's loss before income taxes was $9.2 million and $10.2 million for the years ended December 31, 2016 and 2017, respectively and was generated entirely in the United States. The Company did not record current or deferred income tax expense or benefit during the years ended December 31, 2016 and 2017.

A reconciliation of income tax expense (benefit) to the amount computed by applying the statutory federal income tax rate to the loss from operations is summarized for the years ended December 31, 2016 and 2017, respectively, as follows (in thousands):

| | Year Ended December 31, | |
|---|---|---|
| | 2016 | 2017 |
| Income tax expense (benefit) at statutory rate | $ (3,135) | $ (3,484) |
| State income tax, net of federal benefit | (599) | (528) |
| Permanent items | 2 | 4 |
| Fair value adjustments | — | (164) |
| Non-deductible interest expense | — | 905 |
| Stock-based compensation | 41 | 21 |
| Orphan drug credit | (713) | (616) |
| Research and development credits | (236) | (218) |
| Uncertain tax positions | 237 | 209 |
| Tax Cuts and Jobs Act | — | 10,978 |
| Change in valuation allowance | 4,403 | (7,110) |
| Other | — | 3 |
| Income tax expense (benefit) | $ — | $ — |

Significant components of the Company's deferred tax assets as of December 31, 2016 and 2017, respectively, are shown below:

| | December 31, | |
|---|---|---|
| | 2016 | 2017 |
| Deferred tax assets: | | |
| Net operating loss carryforwards | $ 33,878 | $ 26,138 |
| Research and development credits | 2,989 | 3,863 |
| Accrued expenses | 446 | 239 |
| Intangibles | 131 | 110 |
| Property and equipment | 7 | (2) |
| Other, net | 29 | 22 |
| Total deferred tax assets | 37,480 | 30,370 |
| Valuation allowance for deferred tax assets | (37,480) | (30,370) |
| Deferred tax assets, net of valuation allowance | $ — | $ — |

As of December 31, 2016 and 2017, management assessed the realizability of deferred tax assets and evaluated the need for a valuation allowance against the deferred tax assets. This evaluation utilizes the framework contained in ASC 740, *Income Taxes*, whereby management considers all available positive and negative evidence as of the balance sheet date to determine whether all or some portion of the Company's deferred tax assets will be realized. Under this guidance, a valuation allowance must be established for deferred tax assets when it is more-likely-than-not (a probability level of more than 50%) that the asset will not be realized.

Management followed the guidance in ASC 740, which states that "a cumulative loss in recent years is a significant piece of negative evidence that is difficult to overcome" and concluded that the Company's deferred

tax assets were not realizable as of December 31, 2016 and 2017. Accordingly, a valuation allowance of $37.5 million and $30.4 million has been recorded to offset the deferred tax assets. The change in valuation allowance for the years ended December 31, 2016 and 2017 was an increase of $4.4 million and a decrease of $7.1 million, respectively.

At December 31, 2017, the Company had federal and Pennsylvania net operating loss ("NOL") carryforwards of $91.5 million, and $86.4 million, respectively. The federal and Pennsylvania NOLs may be used to offset future taxable income. The federal and Pennsylvania NOLs will begin to expire in 2022 and 2029, respectively, unless previously utilized.

At December 31, 2017, the Company also has federal and Pennsylvania research and development tax credit carryforwards totaling $3.1 million and $0.1 million, respectively. The federal and Pennsylvania research and development tax credit carryforwards will begin to expire in 2028 and 2029, respectively, unless previously utilized.

At December 31, 2017, the Company also has federal orphan drug credit carryforwards of $2.0 million, which will begin to expire in 2036, unless previously utilized.

For all years through December 31, 2017, we generated a combination of research and development credits and orphan drug credits. Certain of these credits were derived from studies to document the qualified activities and certain other credits were not derived from studies. For the credits that were calculated through a study the IRS, on audit, may disagree with the amount of credits calculated. When studies are ultimately performed for the other credits, they may result in an adjustment to those specific credits. Notwithstanding these potential uncertainties, no amounts are being presented as an uncertain tax position for these years. A full valuation allowance has been provided against our research and development and orphan drug credits and, if adjustments are required, these adjustments to the deferred tax asset established for the research and development and orphan drug credit carryforwards would be offset by an adjustment to the valuation allowance.

Under the Internal Revenue Code, the utilization of a corporation's net operating loss and tax credit carryforwards may be limited following a greater than 50% change in ownership over a three-year period. Any unused annual limitation may be carried forward to future years for the balance of the net operating loss and tax credit carryforward period. Under these rules, prior ownership changes may have created a limitation in the Company's ability to use certain tax carryforwards on a yearly basis. Additionally, certain state operating losses may also be limited, including Pennsylvania, which limits net operating loss carryforward utilization to 30% (35% for 2018 and 40% in 2019 and thereafter) of apportioned taxable income.

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

As a result, the Company believes the most significant impact on its consolidated financial statements will be the reduction of approximately $11.0 million of the deferred tax assets related to net operating losses and other deferred tax assets. Such reduction is offset by a change in the Company's valuation allowance. This impact is considered to be a provisional amount as the Company is still analyzing certain aspects of the Tax Act

and refining its calculations. The ultimate impact may differ from this provisional amount due to, among other things, additional analysis, changes in interpretations and assumptions the Company has made, additional regulatory guidance that may be issued and actions the Company may take as a result of the Tax Act.

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

The Company files income tax returns in the U.S. federal jurisdiction, and various state jurisdictions. Tax years 2014 and forward remain open for examination for federal tax purposes and tax years 2014 and forward remain open for examination for the Company's more significant state tax jurisdictions. To the extent utilized in future years' tax returns, net operating loss carryforwards at December 31, 2017 will remain subject to examination until the respective tax year is closed.

**13. Related Party Transactions**

As described above in Note 11, the Company entered into a license agreement with MedImmune, a related party of the Company.

**14. Subsequent Events**

For the financial statements as of December 31, 2017 and for the year then ended, the Company has evaluated subsequent events through July 27, 2018, the date at which the financial statements were available to be issued, and determined that there are no other items to disclose.

**15. Subsequent Events (unaudited)**

For purposes of the interim unaudited financial statements as of June 30, 2018 and for the six months then ended, the Company has evaluated subsequent events through August 31, 2018, the date at which the interim financial statements were available to be issued.

In July 2018, the SVB Loan was amended to 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 will be extended to December 31, 2018 if the Company draws Tranche C. In August 2018, the Company borrowed $2.0 million under Tranche C.

In August 2018, the Company sold 1,842,959 shares of Series D redeemable convertible 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 convertible notes, including accrued interest thereon, were converted into 2,080,209 shares of Series D. The holders of the Series D are entitled to receive noncumulative cash dividends, on a *pari passu* basis, among the Senior Stock,

Senior Series C Stock and Series D, at the rate of 8% when and if declared by the board of directors. In the event of a liquidation, dissolution or winding up of the company, the holders of the Series D are entitled to be paid an amount equal to $9.659 per share, plus any declared but unpaid dividends, prior and in preference to any distribution to the Preferred Stock or common stock. The holders of the Series D are entitled to a number of votes equal to the number of shares of common stock into which their shares can be converted. The shares of Series D are convertible into an equal number of shares of common stock at the option of the holder, subject to certain anti-dilution adjustments, and are automatically converted into common stock in the event of a Qualified IPO or upon the agreement of 70% of the Series D holders.

**5,000,000 Shares**


**Common Stock**

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**PRELIMINARY PROSPECTUS**

**, 2018**

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**Citigroup** **Cowen** **Stifel**

**Needham & Company**

**Through and including , 2018 (25 days after the commencement of this offering), all dealers that buy, sell or trade shares of our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.**