Bellerophon Therapeutics, Inc.
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Registration Statement No. 333-214230
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PROSPECTUS

17,142,858 Class A Units consisting of Common Stock and Warrants and

3,000 Class B Units consisting of Series A Convertible Preferred Stock and Warrants(1)

(3,529,412 shares of Common Stock underlying the Series A Convertible Preferred Stock)
(17,142,858 shares of Common Stock underlying the Warrants included in the Class A and Class B Units)

We are offering 17,142,858 Class A Units (consisting of one share of our common stock and a warrant to purchase one share of our common stock at an exercise price per full share of common stock equal to $0.80 (each, a "Warrant")). Each Warrant will be immediately exercisable and will expire five years from the date on which such Warrants become exercisable. The shares of common stock and Warrants that form part of a Class A Unit are immediately separable and will be issued separately in this offering.

We are also offering to those purchasers, if any, whose purchase of Class A Units in this offering would otherwise result in the purchaser, together with its affiliates and certain related parties, beneficially owning more than 4.99% of our outstanding common stock immediately following the consummation of this offering, the opportunity, in lieu of purchasing Class A Units, to purchase 3,000 Class B Units. Each Class B Unit will consist of one share of our Series A convertible preferred stock, with a stated value of $1,000 per share and convertible into shares of our common stock at the public offering price of the Class A Units, together with the equivalent number of Warrants as would have been issued to such purchaser if they had purchased Class A Units based on the public offering price. The shares of Series A convertible preferred stock do not generally have any voting rights but are convertible into shares of common stock. The placement agent has informed us that it has not received any indications of interest for Class B Units, thus we do not expect to confirm any sales of such Class B Units. The shares of Series A convertible preferred stock and Warrants are immediately separable and will be issued separately in this offering. We are also offering the shares of common stock that are issuable from time to time upon conversion of the Series A convertible preferred stock and upon the exercise of the Warrants being offered by this prospectus.

For a more detailed description of the Series A convertible preferred stock, see the section entitled "Description of Securities We Are Offering — Series A Convertible Preferred Stock." For a more detailed description of the Warrants, see the section entitled "Description of Securities We Are Offering — Warrants to Purchase Common Stock." For a more detailed description of our common stock, see the section entitled "Description of Capital Stock — Common Stock."

Investors purchasing $100,000 or more of the securities offered hereby will execute a securities purchase agreement with us, providing such investors with certain representations, warranties and covenants from us, which representations, warranties and covenants will not be available to investors of lesser amounts of our securities. Therefore, investors purchasing $100,000 or less of the securities shall rely solely on this prospectus in connection with the purchase of securities in this offering.

We refer to the Series A convertible preferred stock issued hereunder, the Warrants and the shares of common stock issued hereunder and issuable upon conversion of the Series A convertible preferred stock and upon exercise of the Warrants, collectively, as the securities.

Our common stock is listed on the NASDAQ Global Market under the symbol "BLPH." On November 22, 2016, the last reported sale price of our common stock on the NASDAQ Global Market was $0.75 per share. We do not intend to list the Series A convertible preferred stock or the Warrants to be sold in this offering on the NASDAQ Global Market or any other national securities exchange or any other nationally recognized trading system.

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

	Per Class A Unit	Per Class B Unit	Total
Public offering price[1]	$0.7000	$1,000	$12,000,000.60
Placement agent fees[2]	$0.0396	$0	$679,680.04
Proceeds, before expenses, to us	$0.6604	$0	$11,320,320.56

(1) The public offering price is $0.70 per unit.

(2) In addition, we have agreed to reimburse the placement agent for certain expenses. See "Plan of Distribution" on page 75 of this prospectus for additional information.

We have retained H.C. Wainwright & Co., LLC as our exclusive placement agent to use their reasonable best efforts to solicit offers to purchase the securities in this offering. The placement agent has no obligation to buy any of the securities from us or to arrange for the purchase or sale of any specific number or dollar amount of the securities. We expect that delivery of the securities being offered pursuant to this prospectus will be made on or about November 29, 2016.

Entities affiliated with New Mountain Capital, LLC and Linde North America, existing stockholders, have agreed to purchase an aggregate of 7,634,286 Class A Units. The placement agent will receive a fee of 4.0% from any units purchased by these parties.

Investing in our securities involves a high degree of risk. See the section entitled "Risk Factors" appearing on page 8 of this prospectus and elsewhere in this prospectus for a discussion of information that should be considered in connection with an investment in our securities.

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

H.C. Wainwright & Co.

The date of this prospectus is November 22, 2016

(1) The placement agent has informed us that it has not received any indications of interest for Class B Units, thus we do not expect to confirm any sales of such Class B Units.

TABLE OF CONTENTS

Table of Contents

We have not, and the placement agent has not, authorized anyone to provide any information or to make any representations other than those contained in this prospectus or in any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares offered hereby, and only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus or in any applicable free writing prospectus is current only as of its date, regardless of its time of delivery or any sale of our securities. Our business, financial condition, results of operations and prospects may have changed since that date.

For investors outside the United States: We have not, and the placement agent has not, done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose 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 securities and the distribution of this prospectus outside the United States.

Table of Contents

PROSPECTUS SUMMARY

This summary highlights information contained in other parts of this prospectus or incorporated by reference into this prospectus from our filings with the Securities and Exchange Commission, or SEC, listed in the section of the prospectus entitled "Incorporation of Certain Information by Reference." Because it is only a summary, it does not contain all of the information that you should consider before investing in our securities and it is qualified in its entirety by, and should be read in conjunction with, the more detailed information appearing elsewhere or incorporated by reference into this prospectus. You should read the entire prospectus, the registration statement of which this prospectus is a part, and the information incorporated by reference herein in their entirety, including the "Risk Factors" and our financial statements and the related notes incorporated by reference into this prospectus, before investing in our securities. Unless the context requires otherwise, references in this prospectus to "Bellerophon," "we," "us" and "our" refer to Bellerophon Therapeutics, Inc., together with its wholly-owned subsidiaries.

Overview

We are a clinical-stage therapeutics company focused on developing innovative products at the intersection of drugs and devices that address significant unmet medical needs in the treatment of cardiopulmonary diseases. Our focus is the continued development of our nitric oxide therapy for patients with pulmonary hypertension, or PH, using our proprietary delivery system, INOpulse, with pulmonary arterial hypertension, or PAH, representing the lead indication. Our INOpulse platform is based on our proprietary pulsatile nitric oxide delivery device.

In February 2016, we announced positive data from the final analysis of our Phase 2 long-term extension clinical trial of INOpulse for PAH, which is Part 2 of our Phase 2 clinical trial of INOpulse for PAH. The data indicates a sustainability of benefit to PAH patients who received INOpulse therapy at the 75 mcg/kg of ideal body weight/hour dose for an average of greater than 12 hours per day and were on long-term oxygen therapy, or LTOT. After reaching agreement with the U.S. Food and Drug Administration, or FDA, and the European Medicines Agency, or EMA, on our Phase 3 protocol, we are moving forward with Phase 3 development. In September 2015, the FDA issued a Special Protocol Assessment, or SPA, for our Phase 3 PAH program for INOpulse, which will include two confirmatory clinical trials, undertaken either sequentially or in parallel. The first of the two Phase 3 trials has been initiated with the first patient enrolled in June 2016. We plan to have our Data Monitoring Committee conduct an unblinded interim analysis on the first trial after approximately half of the subjects have completed a total of 18 weeks to assess for efficacy, futility and potential sample size reassessment.

We completed a randomized, placebo-controlled, double-blind, dose-confirmation Phase 2 clinical trial of INOpulse for PH-COPD in July 2014. We received results from this trial, and we have initiated further Phase 2 testing to demonstrate the potential benefit on exercise capacity. In September 2015, an oral presentation of late-breaking data

from a clinical trial sponsored by us was presented at the European Respiratory Society International Congress 2015 in Amsterdam. The data showed that INOpulse improved vasodilation in patients with PH-COPD. In July 2016, the results were published in the International Journal of COPD in an article titled "Pulmonary vascular effects of pulsed inhaled nitric oxide in COPD patients with pulmonary hypertension". Building upon this and other work we have done over recent quarters, we have initiated Phase 2 testing for the use of the INOpulse device for PH-COPD patients to evaluate the potential benefit of chronic use on exercise capacity, with the first patient enrolled in October 2016.

We have begun clinical testing of the INOpulse therapy to treat PH associated with idiopathic pulmonary fibrosis, or PH-IPF, based on feedback from the medical community and the large unmet medical need for this condition. Our first patient was enrolled in our Phase 2 study in the second quarter of 2016. In addition, other opportunities for the application of our INOpulse platform include the following indications: chronic thromboembolic PH, or CTEPH, PH associated with sarcoidosis and PH associated with pulmonary edema from high altitude sickness.

We have devoted all of our resources to our therapeutic discovery and development efforts, including conducting clinical trials for our product candidates, protecting our intellectual property and the general and

Table of Contents

administrative support of these operations. We have devoted significant time and resources to developing and optimizing our drug delivery system, INOpulse, which operates through the administration of nitric oxide as brief, controlled pulses that are timed to occur at the beginning of a breath.

To date, we have generated no revenue from product sales. We expect that it will be several years before we commercialize a product candidate, if ever.

Risks Associated with Our Business

Our business and our ability to implement our business strategy are subject to numerous risks, as more fully described in the section entitled “Risk Factors” in our Annual on Form 10-K for the year ended December 31, 2015, incorporated herein by reference. You should read these risks before you invest in our securities. We may be unable, for many reasons, including those that are beyond our control, to implement our business strategy. In particular, risks associated with our business include:

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

- Our very limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

- We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts. Moreover, if we are unable to obtain additional funds on a timely basis, there will be substantial doubt about our ability to continue as a going concern and increased risk of insolvency and loss of investment by our stockholders.

- We are dependent on the success of our INOpulse product candidates and our ability to develop, obtain marketing approval for and successfully commercialize these product candidates. If we are unable to develop, obtain marketing approval for or successfully commercialize our product candidates, either alone or through a collaboration, or experience significant delays in doing so, our business could be materially harmed.

- We rely on Ikaria, as our single source supplier, for our supply of nitric oxide for the clinical trials of INOpulse. Ikaria's inability to continue manufacturing adequate supplies of nitric oxide, or its refusal to supply us with commercial quantities of nitric oxide on commercially reasonable terms, or at all, could result in a disruption in the supply of, or impair our ability to market, INOpulse.

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

- Our product candidates currently in development are exclusively licensed from third parties, and we may enter into additional agreements to in-license technology from third parties. If current or future licensors terminate the applicable license, or fail to maintain or enforce the underlying patents, our competitive position and market share will be harmed.

- We may seek to enter into collaborations with third parties for the development and commercialization of our product candidates. If we fail to enter into such collaborations, or such collaborations are not successful, we may not be able to capitalize on the market potential of our product candidates.

- If we are unable to obtain and maintain patent protection for our technology and products or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be impaired.

Table of Contents

- Our principal stockholders have substantial control over us, which could limit your ability to influence the outcome of key transactions, including any change of control.

Corporate Information

We were incorporated under the laws of the State of Delaware on October 17, 2013 under the name Ikaria Development LLC. We changed our name to Bellerophon Therapeutics LLC on January 27, 2014. On February 12, 2015, we converted from a Delaware limited liability company into a Delaware corporation and changed our name to Bellerophon Therapeutics, Inc. We currently have three wholly-owned subsidiaries: Bellerophon BCM LLC, a Delaware limited liability company; Bellerophon Pulse Technologies LLC, a Delaware limited liability company; and Bellerophon Services, Inc., a Delaware corporation. Our website address is www.bellerophon.com. The information contained on, or that can be accessed through, our website does not constitute part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

Our executive offices are located at 184 Liberty Corner Road, Suite 302, Warren, New Jersey 07059, and our telephone number is (908) 574-4770.

Table of Contents

Implications of Being an Emerging Growth Company and a Smaller Reporting Company

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We will remain an emerging growth company until the earlier of: (i) the last day of the fiscal year in which we have total annual gross revenues of $1 billion or more; (ii) December 31, 2020; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC, which means the first day of the year following the first year in which the market value of our common stock that is held by non-affiliates exceeds $700 million as of June 30. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of reduced reporting burdens in the registration statement of which this prospectus is a part. In particular, we have not included all of the executive compensation information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we rely on certain or all of 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.

In addition, the JOBS Act provides that an emerging growth company may take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we are subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

4

Table of Contents

The Offering

Class A Units offered by us	We are offering 17,142,858 Class A Units. Each Class A Unit will consist of one share of our common stock and a warrant to purchase one share of our common stock at an exercise price per full share of common stock equal to $0.80 (each, a "Warrant"). The Class A Units will not be certificated and the share of common stock and Warrants part of such unit are immediately separable and will be issued separately in this offering.
	This prospectus also relates to the offering of shares of our common stock issuable upon the exercise of the warrants that are part of the Class A Units.
Class B Units offered by us	We are also offering to those purchasers, if any, whose purchase of Class A Units in this offering would otherwise result in the purchaser, together with its affiliates and certain related parties, beneficially owning more than 4.99% of our outstanding common stock immediately following the consummation of this offering, the opportunity, in lieu of purchasing Class A Units, to purchase Class B Units. Each Class B Unit will consist of one share of our Series A convertible preferred stock, with a stated value of $1,000 and convertible into shares of our common stock at the public offering price of the Class A Units, together with the equivalent number of Warrants as would have been issued to such purchaser if they had purchased Class A Units based on the public offering price.
	Ownership of the Class B Units alone will not increase the purchaser's beneficial ownership percentage (up to 9.99%) of common stock unless and until a portion or all of such Series A convertible preferred stock has been converted. In addition, holders of Series A convertible preferred stock will be prohibited from converting Series A convertible preferred stock if, as a result of such conversion, the holder, together with its affiliates and certain related parties, and any persons acting as a group together with such holder or any such affiliate, would beneficially own more than 4.99% of the total number of shares of our outstanding common stock.

However, any holder may decrease or increase such ownership percentage to any other percentage, provided that any increase in such percentage shall not be effective until 61 days after such notice to us. Exceeding 4.99% ownership in shares of our outstanding common stock will trigger certain SEC filing requirements by such holder, including the submission of a Schedule 13G or Schedule 13D, as applicable, while such ownership percentage remains above 4.99%.

Shares of Series A convertible preferred stock do not generally have any voting rights but are convertible into shares of common stock. The Class B Units will not be certificated and the shares of Series A convertible preferred stock and Warrants that are part of such unit are immediately separable and will be issued separately in this offering.

This prospectus also relates to the offering of shares of our common stock issuable upon conversion of the Series A convertible preferred stock and the Warrants part of the Class B Units. The placement agent has informed us that it has not received any indications of interest for Class B Units, thus we do not expect to confirm any sales of such Class B Units.

Warrants	Each Warrant included in the units will have an exercise price per full share of common stock equal to $0.80, will be immediately exercisable and will expire five years from the date on which such Warrants become exercisable.

There is no established public trading market for the warrants, and we do not expect a market to develop. In addition, we do not intend to apply for a listing of the Warrants on any national securities exchange.

Common stock outstanding before this offering	14,559,766 shares
Common stock to be outstanding immediately after this offering	31,702,624 shares

5

Table of Contents

Use of proceeds	We intend to use the net proceeds from this offering for general corporate purposes, including manufacturing expenses, clinical trial expenses, research and development expenses and general and administrative expenses. See "Use of Proceeds."
Risk factors	You should read the "Risk Factors" section of this prospectus for a discussion of certain of the factors to consider carefully before deciding to purchase any securities in this offering.
National Securities Exchange Listing	Our common stock is listed on the NASDAQ Global Market under the symbol "BLPH." We do not intend to list the warrants on any securities exchange or nationally recognized trading system.
No market for the units or Series A convertible preferred stock or warrants	The units will not be certificated, and the securities that are part of such units are immediately separable and will be issued separately in this offering. There is no established public trading market for the Series A convertible preferred stock or the Warrants to be issued in this offering, and we do not intend to apply to list such securities on any securities exchange or automated quotation system.

The number of shares of our common stock to be outstanding immediately after this offering is based on 14,559,766 shares of common stock outstanding as of November 21, 2016 and excludes as of that date:

- 1,444,416 shares of common stock issuable upon the exercise of outstanding stock options at a weighted average exercise price of $6.76 per share;
- 19,385 shares of common stock reserved for future issuance under our 2015 equity incentive plan (the "2015 Equity Incentive Plan"); and
- 17,142,858 shares of our common stock issuable upon the exercise of warrants offered hereby.

Entities affiliated with New Mountain Capital, LLC and Linde North America, existing stockholders, have agreed to purchase an aggregate of 7,634,286 Class A Units.

Table of Contents

Consolidated Summary Financial Data

The following table summarizes certain of our financial data. We derived the consolidated summary statement of operations data for the years ended December 31, 2015 and 2014 from our audited consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2015, incorporated by reference into this prospectus. The consolidated summary statement of operations data for the nine months ended September 30, 2016 and 2015 and the consolidated summary balance sheet data as of September 30, 2016 were derived from our unaudited consolidated financial statements included in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2016, incorporated by reference into this prospectus. The unaudited consolidated financial statements have been prepared on a basis consistent with our audited consolidated financial statements included in this prospectus and include, in our opinion, all normal and recurring adjustments that are considered necessary for the fair presentation of the financial information in those statements. Our historical results are not necessarily indicative of the results that may be expected in the future and results of interim periods are not necessarily indicative of the results for the entire year. The consolidated summary financial data should be read together with our consolidated financial statements and related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in our Annual Report on Form 10-K for the year ended December 31, 2015, incorporated by reference in this prospectus.

	Year Ended December 31		Nine Months Ended September 30	
	2015	2014	2016	2015
Consolidated Statements of Operations Data			(unaudited)	
Operating expenses:				
Research and development	$33, 365	$45,978	$11,539	$25,036
General and administrative	14,870	13,775	4,926	12,337
Total operating expenses	48,235	59,753	16,465	37,373
Other operating income	1,667	—	—	1,667
Loss from operations	(46,568)	(59,753)	(16,465)	(35,706)
Interest income	109	79	74	73
Pre-tax loss	(46,459)	(59,674)	(16,391)	(35,633)
Income tax benefit (expense)	—	—	—	—
Net loss	$(46,459)	$(59,674)	$(16,391)	$(35,633)
Weighted average shares/units outstanding:				
Basic and diluted	12,267,693	7,898,289	13,335,358	12,012,002
Net loss per share/unit:				
Basic and diluted	$(3.79)	$(7.56)	$(1.23)	$(2.97)

The unaudited as -adjusted balance sheet data set forth below give effect to our issuance and sale of shares of our common stock in this offering at the public offering price, after deducting the estimated placement agent fees and expenses and estimated offering expenses payable by us.

	As of September 30, 2016	
	Actual	As adjusted
	(unaudited)	
	(in thousands except share and per share data)	
Consolidated Balance Sheet Data		
Cash and cash equivalents	$ 3,930	$ 14,798
Working capital	12,737	23,605
Total assets	22,784	33,652
Total liabilities	4,788	4,788
Accumulated deficit	(117,069)	(117,069)
Total stockholders' equity	17,996	28,864

Table of Contents

RISK FACTORS

Investing in our securities involves a high degree of risk. You should consider carefully the risks described below, together with all of the other information included or incorporated by reference in this prospectus, including the risks and uncertainties discussed under "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2015, before deciding whether to purchase securities in this offering. All of these risk factors are incorporated herein in their entirety. The risks described below and incorporated by reference are material risks currently known, expected or reasonably foreseeable by us. If any of these risks actually materialize, our business, prospects, financial condition, and results of operations could be seriously harmed. This could cause the trading price of our common stock and the value of the warrants to decline, resulting in a loss of all or part of your investment.

Risks Related to this Offering

There is no public market for the Series A convertible preferred stock or Warrants being offered in this offering.

There is no established public trading market for the Series A convertible preferred stock or the Warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to apply to list the Series A convertible preferred stock or Warrants on any securities exchange or nationally recognized trading system, including the NASDAQ Global Market. Without an active market, the liquidity of the Series A convertible preferred stock and the Warrants will be limited.

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

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section entitled "Use of Proceeds," and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. Our management may not apply the net proceeds from this offering in ways that ultimately increase the value of your investment. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds from this offering in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders. If we do not invest or apply the net proceeds from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

There may be future sales of our securities or other dilution of our equity, which may adversely affect the market price of our common stock.

We are generally not restricted from issuing additional common stock, including any securities that are convertible into or exchangeable for, or that represent the right to receive, common stock. The market price of our common stock could decline as a result of sales of common stock or securities that are convertible into or exchangeable for, or that represent the right to receive, common stock after this offering or the perception that such sales could occur.

Table of Contents

Neither the holders of Warrants purchased in this offering nor the purchasers of the Series A convertible preferred stock will have rights as common stockholders until such holders exercise their warrants and/or preferred stock and acquire our common stock.

Until holders of Warrants and/or purchasers of the Series A convertible preferred stock acquire shares of our common stock upon exercise of the Warrants and/or Series A convertible preferred stock, holders of Warrants and Series A convertible preferred stock will have no rights with respect to the shares of our common stock underlying such Warrants and/or Series A convertible preferred stock. Upon exercise of the Warrants and/or Series A convertible preferred stock, the holders will be entitled to exercise the rights of a common stockholder only as to matters for which the record date occurs after the exercise date.

Even if this offering is successful, we will need to raise additional capital in the future to continue operations, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

We have had recurring losses from operations, negative operating cash flow and an accumulated deficit. We do not generate any cash from operations and must raise additional funds in order to continue operating our business. We expect to continue to fund our operations primarily through equity and debt financings in the future. If additional capital is not available to us when needed or on acceptable terms, we may not be able to continue to operate our business pursuant to our business plan or we may have to discontinue our operations entirely. As of September 30, 2016, we had cash and cash equivalents of $3.9 million. We estimate that we will receive net proceeds of approximately $10.9 million from the sale of the securities offered by us in this offering, and after deducting the estimated placement agent fees and expenses and estimated offering expenses payable by us, and excluding the proceeds, if any, from the exercise of the warrants issued in this offering. We currently anticipate that our existing resources, together with the expected net proceeds from this offering, will be sufficient to fund our planned operations until at least the end of 2017. In the event of a decrease in the net proceeds to us from this offering as a result of a decrease in the assumed public offering price or the number of shares offered by us, based on the assumptions discussed in “Use of Proceeds”, we would expect that our existing resources, together with such reduced expected net proceeds from this offering, would be sufficient to fund our planned operations until at least September 30, 2017.

Developing drugs and conducting clinical trials is expensive. Our future funding requirements will depend on many factors, including:

- the costs and timing of our research and development activities;
- the progress and cost of our clinical trials and other research and development activities;

- the cost and timing of securing manufacturing capabilities for our clinical product candidates and commercial products, if any;

- the terms and timing of any collaborative, licensing, acquisition or other arrangements that we may establish;

- the costs and timing of seeking regulatory approvals;

- the costs of filing, prosecuting, defending and enforcing any patent applications, claims, patents and other intellectual property rights; and

- the costs of lawsuits involving us or our product candidates.

We may seek funds through arrangements with collaborators or others that may require us to relinquish rights to the products candidates that we might otherwise seek to develop or commercialize independently. We cannot be certain that we will be able to enter into any such arrangements on reasonable terms, if at all.

We may seek to raise capital through a variety of sources, including:

Table of Contents

- the public equity market;
- private equity financings;
- collaborative arrangements;
- licensing arrangements; and/or
- public or private debt.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. Our ability to raise additional funds will depend, in part, on the success of our preclinical studies and clinical trials and other product development activities, regulatory events, our ability to identify and enter into in-licensing or other strategic arrangements, and other events or conditions that may affect our value or prospects, as well as factors related to financial, economic and market conditions, many of which are beyond our control. We cannot be certain that sufficient funds will be available to us when required or on acceptable terms, if at all. Raising additional capital through the sale of securities could cause significant dilution to our stockholders. If we are unable to secure additional funds on a timely basis or on acceptable terms, we may be required to defer, reduce or eliminate significant planned expenditures, restructure, curtail or eliminate some or all of our development programs or other operations, dispose of technology or assets, pursue an acquisition of our company by a third party at a price that may result in a loss on investment for our stockholders, enter into arrangements that may require us to relinquish rights to certain of our product candidates, technologies or potential markets, file for bankruptcy or cease operations altogether. Any of these events could have a material adverse effect on our business, financial condition and results of operations. Moreover, if we are unable to obtain additional funds on a timely basis, there will be substantial doubt about our ability to continue as a going concern and increased risk of insolvency and loss of investment by our stockholders.

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference herein contain forward-looking statements. The forward-looking statements are contained principally in the sections entitled "Prospectus Summary," "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business" in this prospectus or the documents incorporated herein by reference. These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- the timing of the ongoing and expected clinical trials of our product candidates, including statements regarding the timing of completion or analysis of the trials and the respective periods during which the results of the trials will become available;
- our ability to obtain adequate financing to meet our future operational and capital needs;
- the timing of and our ability to obtain marketing approval of our product candidates, and the ability of our product candidates to meet existing or future regulatory standards;
- our ability to comply with government laws and regulations;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our estimates regarding the potential market opportunity for our product candidates;
- the timing of or our ability to enter into partnerships to market and commercialize our product candidates;
- the rate and degree of market acceptance of any product candidate for which we receive marketing approval;
- our intellectual property position;
- our estimates regarding expenses, future revenues, capital requirements and needs for additional funding and our ability to obtain additional funding;

- the success of competing treatments;
- our competitive position; and
- our expectations regarding the time during which we will be an "emerging growth company" under the Jumpstart Our Business Startups Act of 2012.

In some cases, you can identify these statements by terms such as "anticipate," "believe," "could," "estimate," "expect," "inten "may," "plan," "potential," "predict," "project," "should," "will," "would" or the negative of those terms, and similar expressio convey uncertainty of future events or outcomes. These forward-looking statements reflect our management's beliefs and views with respect to future events and are based on estimates and assumptions as of the date of this prospectus and are subject to risks and uncertainties. We discuss many of these risks in greater detail in the documents incorporated by reference herein, usually under the heading "Risk Factors." Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. Given these uncertainties, you should not place undue reliance on these forward-looking statements.

You should carefully read this prospectus, the documents that we incorporate by reference into this

Table of Contents

prospectus and the documents 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 the forward-looking statements in this prospectus by these cautionary statements.

Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in any forward-looking statements, whether as a result of new information, future events or otherwise.

Table of Contents

USE OF PROCEEDS

We will receive net proceeds of approximately $10.9 million from the sale of the securities offered by us in this offering after deducting placement agent fees and expenses and estimated offering expenses payable by us and excluding the proceeds, if any, from the exercise of the warrants issued pursuant to this offering and assuming we sell the maximum number of securities we are offering pursuant to the prospectus supplement.

We currently intend to use the net proceeds from this offering for general corporate purposes, including manufacturing expenses, clinical trial expenses, research and development expenses and general and administrative expense.

Our expected use of net proceeds from this offering represents our current intentions based upon our present plans and business condition. As of the date of this prospectus, we cannot currently allocate specific percentages of the net proceeds that we may use for the purposes specified above, and we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the completion of this offering, or the amounts that we will actually spend on the uses set forth above. The amounts and timing of our actual use of the net proceeds will vary depending on numerous factors, including our ability to obtain additional financing, the progress, cost and results of our preclinical and clinical development programs, and whether we are able to enter into future licensing or collaboration arrangements. We may find it necessary or advisable to use the net proceeds for other purposes, and our management will have broad discretion in the application of the net proceeds, and investors will be relying on our judgment regarding the application of the net proceeds from this offering.

Pending the use of the net proceeds from this offering, we intend to invest the net proceeds in investment-grade, interest-bearing instruments.

Table of Contents

PRICE RANGE OF OUR COMMON STOCK

Our common stock has been listed on the NASDAQ Global Market since February 13, 2015 under the symbol "BLPH." Prior to that date, there was no public market for our common stock. As a result, we have not set forth quarterly information with respect to the high and low sales prices for our common stock for the time periods prior to when our stock began to be publicly traded.

On November 22, 2016, the closing price for our common stock as reported on the NASDAQ Global Market was $0.75 per share. The following table sets forth the ranges of high and low sales prices per share of our common stock as quoted on the NASDAQ Global Market.

	High	Low
Year Ended December 31, 2015		
First Quarter (beginning February 13, 2015)	$12.92	$8.01
Second Quarter	$10.88	$7.32
Third Quarter	$8.54	$2.75
Fourth Quarter	$5.09	$2.47
Year Ending December 31, 2016		
First Quarter	$3.75	$1.90
Second Quarter	$4.58	$1.09
Third Quarter	$2.68	$1.24
Fourth Quarter (through November 22, 2016)	$1.48	$0.75

As of November 22, 2016, there were 237 stockholders of record of our common stock. As of such date, the number of shares of our outstanding common stock was 14,559,766. The number of stockholders of record of our voting securities excludes stockholders whose shares were held in nominee or street name by brokers. The actual number of common stockholders is greater than the number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Table of Contents

DIVIDEND POLICY

We have never declared or paid any cash dividends on our common 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.

Table of Contents

CAPITALIZATION

The following table sets forth our cash and cash equivalents and capitalization as of September 30, 2016:

- on an actual basis; and
- on a pro forma as adjusted basis to reflect the sale of 17,142,858 Class A Units being offered in this offering at the public offering price, generating net proceeds of $10.9 million after deducting placement agent fees and expenses and estimated offering expenses payable by us.

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

	As of September 30, 2016	
(In thousands, expect par value) (unaudited)	Actual	As adjusted
Cash and cash equivalents	$ 3,930	$ 14,798
Preferred stock, $0.01 par value per share; 5,000,000 shares authorized, zero shares issued and outstanding actual, and as adjusted	—	—
Common stock, $0.01 par value per share; 125,000,000 shares authorized, 14,506,997 shares issued and outstanding actual, and 31,702,624 shares issued and outstanding as adjusted	145	317
Additional paid-in capital	134,921	145,617
Accumulated other comprehensive loss	(1)	(1)
Accumulated deficit	(117,069)	(117,069)
Total stockholders’ equity	17,996	28,864
Total capitalization	17,996	28,864

Table of Contents

BUSINESS

Overview

We are a clinical-stage therapeutics company focused on developing innovative products at the intersection of drugs and devices that address significant unmet medical needs in the treatment of cardiopulmonary diseases. Our focus is the continued development of our nitric oxide therapy for patients with pulmonary hypertension, or PH, using our proprietary delivery system, INOpulse, with pulmonary arterial hypertension, or PAH, representing the lead indication. Our INOpulse platform is based on our proprietary pulsatile nitric oxide delivery device.

In February 2016, we announced positive data from the final analysis of our Phase 2 long-term extension clinical trial of INOpulse for PAH, which is Part 2 of our Phase 2 clinical trial of INOpulse for PAH. The data indicates a sustainability of benefit to PAH patients who received INOpulse therapy at the 75 mcg/kg of ideal body weight/hour dose for an average of greater than 12 hours per day and were on long-term oxygen therapy, or LTOT. After reaching agreement with the U.S. Food and Drug Administration, or FDA, and the European Medicines Agency, or EMA, on our Phase 3 protocol, we are moving forward with Phase 3 development. In September 2015, the FDA issued a Special Protocol Assessment, or SPA, for our Phase 3 PAH program for INOpulse, which will include two confirmatory clinical trials, undertaken either sequentially or in parallel. The first of the two Phase 3 trials has been initiated with the first patient enrolled in June 2016. We plan to have our Data Monitoring Committee conduct an unblinded interim analysis on the first trial after approximately half of the subjects have completed a total of 18 weeks to assess for efficacy, futility and potential sample size reassessment.

We completed a randomized, placebo-controlled, double-blind, dose-confirmation Phase 2 clinical trial of INOpulse for PH-COPD in July 2014. We received results from this trial, and we have initiated further Phase 2 testing to demonstrate the potential benefit on exercise capacity. In September 2015, an oral presentation of late-breaking data from a clinical trial sponsored by us was presented at the European Respiratory Society International Congress 2015 in Amsterdam. The data showed that INOpulse improved vasodilation in patients with PH-COPD. In July 2016, the results were published in the International Journal of COPD in an article titled "Pulmonary vascular effects of pulsed inhaled nitric oxide in COPD patients with pulmonary hypertension". Building upon this and other work we have done over recent quarters, we have initiated Phase 2 testing for the use of the INOpulse device for PH-COPD patients to evaluate the potential benefit of chronic use on exercise capacity, with the first patient enrolled in October 2016.

We have begun clinical testing of the INOpulse therapy to treat PH associated with idiopathic pulmonary fibrosis, or PH-IPF, based on feedback from the medical community and the large unmet medical need for this condition. Our first patient was enrolled in our Phase 2 study in the second quarter of 2016. In addition, other opportunities for the application of our INOpulse platform include the following indications: chronic thromboembolic PH, or CTEPH, PH associated with sarcoidosis and PH associated with pulmonary edema from high altitude sickness.

We have devoted all of our resources to our therapeutic discovery and development efforts, including conducting clinical trials for our product candidates, protecting our intellectual property and the general and administrative support of these operations. We have devoted significant time and resources to developing and optimizing our drug delivery system, INOpulse, which operates through the administration of nitric oxide as brief, controlled pulses that are timed to occur at the beginning of a breath.

To date, we have generated no revenue from product sales. We expect that it will be several years before we commercialize a product candidate, if ever.

Our Development Program

The following table summarizes key information about our primary development product, INOpulse, and indications for which we have worldwide commercialization rights.

Table of Contents

From the inception of our business through December 31, 2015, $228.0 million was invested in our development programs. Prior to our February 2015 initial public offering, or IPO, our sole source of funding was investments in us by our former parent company, Ikaria, Inc. (a subsidiary of Mallinckrodt plc), or Ikaria. As used herein, unless the context otherwise requires, references to “Ikaria” refer to Ikaria, Inc. and its subsidiaries and any successor entity.

INOpulse

Our INOpulse program is an extension of the technology used in hospitals to deliver continuous-flow inhaled nitric oxide. Use of inhaled nitric oxide is approved by the U.S. Food and Drug Administration, or the FDA, and certain other regulatory authorities to treat persistent PH of the newborn. Ikaria has marketed continuous-flow inhaled nitric oxide as INOmax for hospital use in this indication since FDA approval in 1999. In October 2013, Ikaria transferred to us exclusive worldwide, royalty-free rights to develop and commercialize pulsed nitric oxide in PAH, PH associated with chronic obstructive pulmonary disease, or PH-COPD, and PH associated with idiopathic pulmonary fibrosis, or PH-IPF. In July 2015, we expanded the scope of our license to allow us to develop our INOpulse program for the treatment of chronic thromboembolic PH, or CTEPH, PH associated with sarcoidosis and PH associated with pulmonary edema from high altitude sickness with a royalty equal to 5% of net sales of any commercial products for these three additional indications. In November 2015, we entered into an amendment to our exclusive cross-license, technology transfer and regulatory matters agreement with Ikaria that included a royalty equal to 3% of net sales of any commercial products for PAH. Our INOpulse program is built on scientific and technical expertise developed for the therapeutic delivery of inhaled nitric oxide. In 2010 and 2012, respectively, Ikaria submitted investigational new drug applications, or INDs, for INOpulse for the treatment of patients with PAH and PH-COPD. PAH is a form of PH that is closely related to persistent PH of the newborn. These INDs were included in the assets that were transferred to us by Ikaria.

Nitric oxide is naturally produced and released by the lining of the blood vessels and results in vascular smooth muscle relaxation, an important factor in regulating blood pressure. Relaxation of the muscles of the blood vessels allows the heart to increase blood flow to tissues and organs of the body, including the lung. When administered through inhalation, nitric oxide acts to selectively reduce pulmonary arterial pressure in the lung with minimal effects on blood pressure outside of the lungs, an important safety consideration.

Inhaled nitric oxide is widely used in the hospital setting for the treatment of a variety of conditions and, as reported by Ikaria, over 600,000 patients have been treated with inhaled nitric oxide worldwide since its first such use. However, chronic outpatient use of this therapy has previously been limited by a lack of a safe and compact delivery system for outpatient use. We have designed our INOpulse device, which is the means by which inhaled nitric oxide is delivered to the patient, to be portable, which enables use by ambulatory patients on a daily basis inside or outside their homes. Our INOpulse device has a proprietary mechanism that delivers brief, targeted pulses of nitric oxide

timed to occur at the beginning of a breath for delivery to the well-ventilated alveoli of the lungs, which minimizes the amount of drug required for treatment. We estimate this, and the higher concentration of nitric oxide we use, reduces the volume of drug delivered to approximately 5% of the volume required for equivalent alveolar absorption using standard continuous flow delivery systems, and also reduces the amount of nitric oxide, as well as its by-product nitrogen dioxide, that is exhaled and released into the patient's environment. INOpulse is designed to automatically adjust nitric oxide delivery based on a patient's breathing pattern to deliver a constant and

Table of Contents

appropriate dose of the inhaled nitric oxide over time, independent of the patient's activity level, thus ensuring more consistent dosing of the nitric oxide to the alveoli of the lungs.

In our recently completed INOpulse clinical trials, we used the first generation INOpulse device, which we refer to as the INOpulse DS device. Beginning with our Phase 3 trial of INOpulse for PAH in 2016, we have begun using our second generation device, which we refer to as the INOpulse device. The INOpulse device has approximately the same dimensions as a paperback book and weighs approximately 2.5 pounds. The INOpulse device has a simple and intuitive user interface and a battery life of approximately 16 hours when recharged, which takes approximately four hours and can be done while the patient sleeps. Based on the doses we have evaluated in our clinical trials, we expect that most patients will use two cartridges a day. The INOpulse device incorporates our proprietary triple-lumen nasal cannula, safety systems and proprietary software algorithms. The triple-lumen nasal cannula enables more accurate dosing of nitric oxide and minimizes infiltration of oxygen, which can react with nitric oxide to form nitrogen dioxide. Our triple-lumen nasal cannula consists of a thin, plastic tube that is divided into three channels from end-to-end, including at the prongs that are placed in the patient's nostrils, with one channel delivering inhaled nitric oxide, a second for breath detection and a third available for oxygen delivery. INOpulse is configured to be highly portable and compatible with long-term oxygen therapy, or LTOT, systems via nasal cannula delivery.

The INOpulse device has been well received by patients in the usability research we have conducted. In addition to the baseline testing on the original INOpulse DS device, we have conducted two rounds of testing with COPD and PAH patients to evaluate the user interface, loading mechanism, size, carrying bag and other features. In the usability research we have conducted, all eight patients with experience with the INOpulse DS device responded positively to the INOpulse device, and several of these patients indicated that the ability to take the INOpulse device outside the home would likely reduce concerns with maintaining compliance.

Our technology is based on patents we have exclusively licensed from Ikaria for the treatment of PAH, PH-COPD, PH-IPF, CTEPH, PH associated with sarcoidosis and PH associated with pulmonary edema from altitude sickness which, collectively, we refer to as the Bellerophon indications. These include patents with respect to the pulsed delivery of nitric oxide to ensure a consistent dose over time, which expire as late as 2027 in the United States and as late as 2026 in certain other countries, as well as with respect to the special triple-lumen cannula that allows for safer and more accurate dosing of pulsed nitric oxide, which expires in 2033 in the United States and abroad. We have also licensed several other patent applications from Ikaria for certain of the innovations included in the INOpulse device and certain of the resulting patents, if issued, would expire as late as 2030 in the United States.

During January 2016, the European Patent Office issued a Notice of Intention to Grant a European Patent that provides protection for our INOpulse program. The patent, entitled "System of Administering a Pharmaceutical Gas to a Patient," covers the ability to provide a known amount of pharmaceutical gas to a patient regardless of the patient inspiration rate or volume and distinguishes the INOpulse® delivery system from others on the market. Upon grant by the European Patent Office, the patent can be officially validated in up to 38 European countries. Also during January 2016, we received EC Certification for our proprietary new, INOpulse® drug-device delivery system. This European

Conformity, or EC Certification grants CE marking on the INOpulse product, which confirms INOpulse compliance with the essential requirements of the relevant European health, safety and environment protection legislation of the European Union. This certification covers the design, development and manufacture of inhaled pulsatile nitric oxide drug delivery systems including our triple-lumen cannula and application software.

INOpulse for PAH

We are developing INOpulse for the treatment of PAH to address a significant and unmet medical need in an orphan disease, which is a disease that affects fewer than 200,000 individuals in the United States. This program represents a potential first-in-class therapy for this indication. In 2011, the FDA granted orphan drug designation to our nitric oxide program for the treatment of PAH. If a product with an orphan drug designation is the first to receive FDA approval, the FDA will not approve another product for the same indication that uses the same active ingredient for seven years, except in a limited number of specific situations such as another product being shown to be clinically superior.

Table of Contents

PAH is characterized by abnormal constriction of the arteries in the lung that increases the blood pressure in the lungs which, in turn, results in abnormal strain on the heart's right ventricle, eventually leading to heart failure. While prevalence data varies widely, we estimate that there are a total of at least 35,000 patients currently diagnosed with and being treated for PAH in the United States and European Union. Moreover, because PAH is rare and causes varied symptoms, we believe there is significant under-diagnosis of the condition at its early stages. There are several approved therapies for PAH, and we estimate, based on public product sales data, that 2014 combined global sales for these therapies were over $4.6 billion with a compounded annual growth rate of approximately 7%. Most PAH patients are treated with multiple medications and many are on supportive therapy. We believe that 40 to 60% of PAH patients are on LTOT. Despite the availability of multiple therapies for this condition, PAH continues to be a life-threatening, progressive disorder. A French registry initiated in 2002 and a U.S. registry initiated in 2006 estimate that the median survival of patients with PAH is three and five years from initial diagnosis, respectively.

We completed a randomized, placebo-controlled, double-blind Phase 2 clinical trial of INOpulse for PAH in October 2014, which was Part 1 of the trial. In February 2016, we announced positive data from the final analysis of Part 2 of our Phase 2 clinical trial of INOpulse for PAH. The data reinforces the results from October 2014 and indicates a sustainability of benefit to PAH patients who received INOpulse therapy at the 75 mcg dose for an average of greater than 12 hours per day and were also treated with LTOT. After reaching agreement with the FDA, and the European Medicines Agency, or EMA, on our Phase 3 protocol, we are moving forward with Phase 3 development. In September 2015, the FDA issued a Special Protocol Assessment, or SPA, for our Phase 3 PAH program for INOpulse, which will include two confirmatory clinical trials, undertaken either sequentially or in parallel. The first of the two Phase 3 trials has been initiated with the first patient enrolled in June 2016. We plan to have our Data Monitoring Committee conduct an un-blinded interim analysis on the first trial after approximately half of the subjects have completed a total of 18 weeks to assess for efficacy, futility and potential sample size reassessment.

INOpulse for PH-COPD

We are also developing INOpulse for the treatment of PH-COPD. COPD is a disease characterized by progressive and persistent airflow limitations. Patients with more severe COPD frequently have hypoxemia, or an abnormally low level of oxygen in the blood, and may be treated with LTOT. Despite treatment with oxygen, hypoxemia can progress and contribute to PH. In 2010, Datamonitor estimated that over 1.4 million COPD patients in the United States were being treated with LTOT. Based on academic studies, we estimate that 50% of COPD patients on LTOT have PH. PH-COPD patients have a lower median life expectancy and a higher rate of hospitalization than COPD patients with similar respiratory disease but without PH. Currently, there are no approved therapies for treating PH-COPD, and the only generally accepted treatments are LTOT, pulmonary rehabilitation and lung transplant. The overall COPD market in the United States was estimated to be approximately $32 billion in 2010 with a compounded annual growth rate of approximately 4%.

The data from an initial three-month, open-label chronic-use Phase 2 trial conducted by a third party, which we in-licensed, showed that pulsed inhaled nitric oxide significantly reduced pulmonary arterial pressures in PH-COPD

patients on LTOT and did so without causing hypoxemia, which is a significant concern for these patients. The FDA asked us to confirm the dose range and the safety related to hypoxemia in PH-COPD patients using the INOpulse device, prior to proceeding to large scale trials. Following this guidance, we conducted a Phase 2 acute dose ranging randomized placebo-controlled trial in 159 patients with the INOpulse DS device, with doses ranging from 3 mcg to 75 mcg. This trial, which we completed in July 2014, identified a dose range that showed similar reduction in pulmonary arterial pressure versus baseline when compared to the initial acute effects of pulsed inhaled nitric oxide in the original chronic-use trial. In addition, in our confirmatory trial, none of the INOpulse doses tested had an adverse effect on hypoxemia relative to placebo. While the reduction in pulmonary arterial pressure did not reach statistical significance versus placebo in this acute setting, which was the primary endpoint of the trial, we believe that the results have confirmed a dose range for this therapy that delivers a significant reduction in pulmonary arterial pressure versus baseline and does not cause hypoxemia in patients with PH-COPD. In September 2015, an oral presentation of late-breaking data from a clinical trial sponsored by us was presented at the European Respiratory Society International Congress 2015 in Amsterdam. The data showed that INOpulse improved vasodilation in patients with PH-COPD. Building upon this and other work we have done over recent quarters, we have initiated additional Phase 2 testing for the use of the INOpulse device for PH-COPD patients to evaluate the potential benefit of chronic use on exercise capacity, with the first patient enrolled in October 2016.

Table of Contents

Our Strategy

Our goal is to become a leader in developing and commercializing innovative products at the intersection of drugs and devices that address significant unmet medical needs in the treatment of cardiopulmonary diseases. The key elements of our strategy to achieve this goal include:

- *Advance the clinical development of INOpulse.* One of our lead indications for our product candidate is INOpulse for PAH. Our Phase 3 PAH program for INOpulse will include two confirmatory clinical trials, undertaken either sequentially or in parallel, with the first patient enrolled in June 2016. We also initiated our second Phase 2 study for INOpulse in PH-COPD looking at the effect of chronic use on exercise capacity, for which the first patient was enrolled in October 2016. We also initiated our Phase 2 studies in PH-IPF consisting of an exploratory acute hemodynamic study, for which the first patient was enrolled in second quarter of 2016, to be followed by exercise capacity.

- *Leverage our historical core competencies to expand our pipeline.* Our employees have years of institutional experience in the use of inhaled nitric oxide in treating PH and in the development of drug-device combination product candidates. If we successfully advance INOpulse, we expect to develop INOpulse for treatment of CTEPH, PH associated with sarcoidosis and PH associated with pulmonary edema from altitude sickness and, subject to obtaining additional license rights from Ikaria, potentially other outpatient PH indications. Our longer-term vision is to identify and opportunistically in-license innovative therapies that are at the intersection of drugs and devices and to develop and commercialize these product candidates.

- *Build commercial infrastructure in select markets.* As we near completion of the development of our product candidates, we may build a commercial infrastructure to enable us to market and sell certain of our product candidates with a specialized sales force and to retain co-promotion or similar rights, when feasible, in indications requiring a larger commercial infrastructure. While we may partner with third parties to commercialize our product candidates in certain countries, we may also choose to establish commercialization capabilities in select countries outside the United States.

INOpulse

INOpulse Scientific Background

Nitric oxide is a naturally occurring molecule produced by many cells of the body. Researchers found that nitric oxide is produced and released by the lining of the blood vessels and plays a role in controlling muscle tone in blood vessels. In particular, nitric oxide results in vascular smooth muscle relaxation in blood vessels and thus is an important factor

in regulating blood pressure. As the muscles of the blood vessels relax, blood flow increases, helping the heart to deliver more blood to the body. PH patients can have a deficiency in endogenous nitric oxide production in their lungs. When administered by inhalation to patients with PH, we expect inhaled nitric oxide to act in a similar manner to naturally produced nitric oxide.

The scientific journal *Science* named nitric oxide Molecule of the Year in 1992. Additionally, the three researchers who discovered the role of nitric oxide as a signaling molecule in the cardiovascular system earned the Nobel Prize for Physiology or Medicine in 1998.

In 1991, Dr. Warren Zapol and his associates at the Massachusetts General Hospital discovered that inhaling nitric oxide in gas form could reduce high blood pressure in the lungs, a condition known as PH. Nitric oxide is a rapid and potent vasodilator, which means it dilates, or widens, blood vessels. When inhaled, it quickly dilates blood vessels in the lungs, which reduces blood pressure in the lungs, strain on the right ventricle and shunting of de-oxygenated blood away from the lungs. Because more blood can flow through the lungs, oxygen levels within blood improve. In addition, inhaled nitric oxide improves the efficiency of oxygen delivery, and because it is a gas, it goes only to the portions of the lung that are ventilated, or receiving air flow, and increases blood flow only in these areas. Thus, inhaled nitric oxide improves ventilation-perfusion matching, an important

Table of Contents

element of lung function involving the air that reaches the lungs, or ventilation, and the blood that reaches the lungs, or perfusion. Inhaled nitric oxide is quickly inactivated after contact with blood, and is selective for the lungs, meaning that it has minimal effects on blood pressure outside of the lungs, which is an important safety consideration.

In 1999, the FDA approved the use of inhaled nitric oxide for the short-term treatment of persistent PH of the newborn. Based on this approval, and similar approvals from foreign regulatory authorities, continuous-flow inhaled nitric oxide, which is administered to ventilated patients by a dedicated in-hospital device, is marketed by Ikaria and its commercialization partners worldwide as INOmax (INOflo in Japan). Inhaled nitric oxide is widely used in the hospital setting for a variety of conditions and, as reported by Ikaria, over 600,000 patients have been treated with inhaled nitric oxide worldwide since its commercial launch. However, chronic outpatient use of this therapy has previously been limited by the lack of a safe and compact delivery system for outpatient use.

Introduction to Pulmonary Hypertension

PH is a disease characterized by constriction of the blood vessels in the lung, which causes blood pressure in the lung to rise and, in turn, increases the work required for the right ventricle of the heart to pump blood. The World Health Organization, or WHO, has endorsed a consensus classification for PH that was updated most recently in 2013. The WHO classification has five broad PH groups based on similarities in pathological and hemodynamic characteristics and therapeutic approaches. We are initially focusing development of INOpulse in indications included in WHO Groups 1 and 3 due to our view of the likelihood of success and the size and commercial viability of these markets. Group 1 PH is comprised of patients with PAH. This Group combines conditions with a range of causes, all of which have a characteristic pattern of vascular remodeling. The constriction of the blood vessels and the resulting pressure on the heart is often the major reason for poor prognosis of PAH patients since they can be otherwise healthy. Most PAH-specific medications are vasodilators and work through one of the three key mechanistic pathways for vasoconstriction and vasodilation. We expect that, because inhaled nitric oxide is a vasodilator and PH patients can have a deficiency in endogenous nitric oxide production in their lungs, patients in Group 1 will benefit from INOpulse. Group 3 PH consists of PH associated with lung disease or hypoxemia, which is an abnormally low level of oxygen in the blood. This Group includes patients with PH-COPD and PH-IPF, among others.

INOpulse for Pulmonary Arterial Hypertension

We are developing INOpulse for PAH to address a significant and unmet medical need in an orphan disease. This product candidate represents the development of a potential first-in-class therapy for this indication. Although current therapy for PAH provides some therapeutic benefit, there remains no cure, and approved therapies can have significant systemic side effects, such as hypotension and liver injury. INOpulse for PAH is designed to be a selective, short-acting pulmonary vasodilator and is being tested as an add-on therapy to existing PAH medications to evaluate its efficacy and side effect profile, in particular its ability to provide clinical benefit without adding to the systemic

effects of other therapies such as hypotension.

Disease Background and Market Opportunity

PAH is a life-threatening, progressive disorder characterized by abnormally high blood pressure, or hypertension, in the pulmonary artery, the blood vessel that carries blood from the heart to the lungs. PAH occurs when most of the very small arteries, or arterioles, throughout the lungs narrow in diameter, which increases the resistance to blood flow through the lungs. To overcome the increased resistance, pressure increases in the pulmonary artery and the right ventricle, which is the heart chamber that pumps blood into the pulmonary artery. In addition, PAH may cause changes to the blood vessel lining that hinder the natural production of nitric oxide. Signs and symptoms of PAH occur when this increased pressure in the right

ventricle cannot fully overcome the elevated resistance.

There are a number of drugs approved for the treatment of PAH that work primarily by reducing pulmonary vascular resistance, which is the primary problem for these patients. The currently approved PAH medications slow down disease progression, but do not prevent the underlying disease. Despite the availability of multiple therapies for this condition, the mortality rate for PAH remains high, with estimates of median survival ranging from three to five years. Currently, the only definitive treatment for PAH is a lung transplant, which is only available to a minority of patients due to the strict requirements and availability of viable lungs for transplant. Patients with PAH also report severe impairment of health-related quality of life, including poor

Table of Contents

general and emotional health and impaired physical functioning. The most common symptoms of PAH are shortness of breath during exertion and syncope, or fainting spells. People with PAH may experience additional symptoms, particularly as the condition worsens, including dizziness, swelling of the ankles or legs, chest pain and a racing pulse. These impairments to health-related quality of life are comparable and sometimes more severe than those reported in patients with severely debilitating conditions such as spinal cord injury.

Since PAH is an orphan condition with poor diagnosis rates, published prevalence estimates for PAH vary widely. Based on epidemiological studies and current treatment rates, we estimate that there are a total of at least 35,000 patients currently diagnosed and treated for PAH in the United States and European Union. The average age of PAH patients at diagnosis is approximately 50 years, and approximately 80% of PAH patients are female. PAH is often diagnosed late in the disease progression with approximately 73% of these patients already having progressed to WHO functional Class III or IV at the time of diagnosis.

PAH is characterized by abnormal constriction of the arteries in the lung. PAH patients are generally treated with one or more of the four major classes of approved medications, which are prostacyclin and prostacyclin analogs, phosphodiesterase type-5 inhibitors, endothelin receptor antagonists and a soluble guanylate cyclase stimulator, all of which potentially result in vasodilatory systemic effects and, therefore, hypotension. Current guidelines recommend treatment with multiple medications in Class III and IV patients with progressive disease but suggest treatment be carefully managed by experienced physicians. Approximately 45% of PAH patients are treated with more than one class of medication at a given time. In addition, since hypoxemia can be a problem in these patients, it is often treated with LTOT in accordance with broadly supported treatment guidelines in the United States and European Union.

We are testing INOpulse for PAH as an add-on therapy for use in patients whose disease is progressing and who use additional medications. If it is approved, we expect INOpulse will provide the greatest benefit to patients who require pulmonary arterial pressure reductions beyond the reductions achieved with the medication they are already using. Because of its localized effect and short-half life, we do not expect INOpulse will add to systemic blood pressure reductions of other PAH drugs. We believe that INOpulse is also likely to be preferentially prescribed for patients already on LTOT. Data from the REVEAL registry, a registry study of PAH based in the United States, indicate that approximately 40% of patients are treated with oxygen for hypoxemia. A more recent assessment of the use of oxygen in the REVEAL registry found that 57% of PAH patients were on LTOT. Approximately 60% of the patients from Part 1 of our Phase 2 clinical trial completed in October 2014 were on LTOT. We believe that, as compared to patients who are not using a nasal cannula, patients who are accustomed to using a nasal cannula for delivery of oxygen are more likely to be prescribed and are more likely to be compliant with the use of INOpulse.

A 2013 report by CVS Caremark Specialty Analytics provided examples of PAH medications with annual prices ranging from approximately $100,000 to $150,000 per patient per year in the United States. We expect that, if approved, the price of INOpulse will be in the range of other established PAH medications.

Scientific Rationale for Use of INOpulse for PAH

Since the discovery of the significant role of nitric oxide in vasodilation, there has been an expectation in the scientific community that inhaled nitric oxide could be an effective therapy for PAH. According to the Cleveland Clinic Center for Continuing Education section on Pulmonary Hypertension, exogenous administration of nitric oxide by inhalation is probably the most effective and specific therapy for PAH, but cost and technical complexity of delivering inhaled nitric oxide have limited its use to the hospital. Although not approved for the treatment of PAH, data from an in-hospital survey conducted by Ikaria showed an estimated 1,000 to 2,000 INOmax uses in PAH patients in the United States each year, indicating that physicians already use nitric oxide in some PAH patients. The difficulty in delivering inhaled nitric oxide outside of the hospital results from the size of the device and cylinder and the need for a specialized delivery system with built-in safety systems.

We are developing nitric oxide for treatment of PAH because nitric oxide is a proven vasodilator, and PAH is primarily a disease of high pulmonary vascular resistance. PAH is associated with impaired release of nitric oxide and thus we believe chronic administration of inhaled nitric oxide may be viewed as an adjunctive or replacement therapy in patients with PAH. The use of inhaled nitric oxide in PAH has been proposed since the role of nitric

Table of Contents

oxide in this disease was identified. This drug has been tested in limited investigational studies conducted at academic institutions.

One clinical trial conducted by a third party at an academic center in Spain in 11 patients, seven of whom had severe PAH and four of whom had severe chronic thromboembolic PH, or CTEPH, evaluated the use of pulsed inhaled nitric oxide in an ambulatory setting. In this open-label, single-arm trial with no placebo control, patients were given ambulatory pulsed inhaled nitric oxide therapy via a nasal cannula for up to one year, after being withdrawn from PAH-specific therapy. The nitric oxide pulse was delivered to the patient at the beginning of each inspiration at a flow rate that was individualized for such patient. The goal of this trial was to evaluate the efficacy and safety of long-term treatment with inhaled nitric oxide outside the hospital setting.

At the start of this trial, patients were evaluated for various measures including the distance they were able to walk in six minutes and their WHO functional class status. At baseline, most of these patients had significant impairment of six-minute walk distance, or 6MWD, with the ability to walk an average of 125 meters, and poor WHO functional class status, with nine patients in Class IV and two patients in Class III. After one month of therapy, overall, patients improved based on WHO functional class, with six patients in Class III and five in Class II, and had improvements in 6MWD of 128 meters on average. After six months of treatment, patients did not worsen clinically, however, between months six and 12, seven patients were given a phosphodiesterase type-5 inhibitor due to clinical worsening. One patient who initially did well with the added phosphodiesterase type-5 inhibitor therapy developed severe right heart failure at month eight and died, and another patient received a lung transplant at month nine. The remaining nine patients all had clinical status at month 12 similar to their one month evaluation, and improvements in functional class and 6MWD for the group persisted over time.

We do not expect INOpulse to have systemic effects beyond the pulmonary vasculature because of the short half-life of nitric oxide combined with its targeted delivery to the alveoli. When nitric oxide is delivered as a pulse at the beginning of inhalation, it travels to the alveoli where it diffuses rapidly across the alveolar capillary membrane into the adjacent vascular smooth muscle of pulmonary vessels. This transport is similar to the natural transport of endogenous nitric oxide from the endothelial cells, where it is produced, to the vascular smooth muscle cells where it relaxes the muscle and causes vasodilation of the pulmonary arteries. We believe this makes INOpulse unlikely to have intolerable side effects, such as systemic hypotension or drug-drug interactions. Given the need for PAH patients to be treated with multiple therapies and the potential for increased hypotension from each of the currently approved PAH therapies, we are developing INOpulse as an add-on or adjunctive therapy for PAH, where we believe it has the highest commercial potential.

Clinical Development Program

INOpulse for PAH is designated as a drug-device combination by the FDA and is subject to review by the Division of Cardiovascular and Renal Products within the Center for Drug Evaluation and Research with consultation from the Center for Devices and Radiological Health. Based upon our IND for PAH, the FDA has agreed that no further preclinical studies are required for clinical development of INOpulse for PAH.

Phase 2 Clinical Trial

In October 2014, we completed Part 1 of our ongoing Phase 2 clinical trial of INOpulse for PAH in the United States and Canada. Our key inclusion criteria for patients in this trial were that they be diagnosed with PH WHO Group 1, be on at least one other PAH medication for at least 12 weeks prior to treatment with INOpulse; and demonstrate being able to walk between 100 and 450 meters within six minutes. In addition, this trial excluded patients with evidence of significant left ventricular dysfunction.

The trial was a randomized, placebo-controlled, double-blind clinical trial with patients randomized 1:1:1 to placebo or to one of two active doses, either 25 or 75 mcg/kg ideal body weight/hour, (iNO 25 or iNO 75), for 16 weeks. The primary endpoint in this trial was a change in pulmonary vascular resistance from baseline to 16 weeks, which was the end of Part 1. The target change in pulmonary vascular resistance was 190 dynes sec. cm-5, and the trial was powered for statistical significance at 130 dynes sec. cm-5. The main secondary endpoint was change in 6MWD over the same period. A clinically meaningful change in 6MWD is typically considered to be an increase of at least 30 to 35 meters.

Table of Contents

We randomized 80 patients for Part 1 of the Phase 2 clinical trial. The majority of the patients were female (79%), white (89%) and had idiopathic PAH (74%). The results from Part 1 of this trial, showed a trend toward lower pulmonary vascular resistance in both the active arms compared to placebo and a trend toward increased 6MWD in the higher dose group. However, neither result was statistically significant.

However, among LTOT users, there was a clinically meaningful and statistically significant improvement versus placebo in both pulmonary vascular resistance and 6MWD in patients on the iNO75 dose.

The Part 1 data analysis showed the following:

- Patients on LTOT in the iNO 75 dose treatment arm who remained on INOpulse therapy for at least 12 hours a day had a mean improvement of 52.4 meters as compared to baseline (n=13).

- Patients on LTOT in the iNO 75 dose treatment arm who remained on INOpulse therapy for less than 12 hours a day showed a mean decrease of 10.7 meters as compared to baseline (n=5).

- Patients on LTOT in the iNO 25 dose treatment arm had a mean increase of 9.1 meters from baseline (n=15).

- Patients on LTOT in the Placebo arm had a mean decrease of 10.7 meters from baseline (n=10).

The patients on LTOT in the iNO 75 dose treatment arm who remained on the INOpulse therapy for at least 12 hours a day had a placebo corrected increase of 69.6 meters (increase of 52.4 meters for iNO 75 against a decrease of 17.2 meters for the corresponding placebo arm).

INOpulse was relatively well-tolerated in Part 1 of this trial. Our Independent Data Safety Monitoring Board evaluated the safety analysis from Part 1 of the trial in November 2014 and recommended proceeding with Part 2 of the trial. Possibly drug-related serious adverse events, or SAEs, occurred in no patients in the placebo group and one subject in each of the iNO25 and iNO75 groups.

One patient in the placebo arm died during Part 1 of the trial due to worsening PAH. SAEs were reported for four patients in the placebo arm, including one each of: pneumonia/worsening PAH, catheter-related infection, ascites and left hip sciatica. Each of these was assessed by the investigator for the trial as unrelated. Four patients in the iNO25 low-dose active treatment arm experienced SAEs, including bacteremia, myelodysplastic syndrome, increased

shortness of breath and dyspnea, one of which was assessed as possibly related to trial therapy. The iNO75 high-dose active treatment arm had nine patients with SAEs. The most common SAEs reported in the iNO75 group were syncope and bronchitis/tracheobronchitis, one of which was assessed as possibly related to trial therapy. Discontinuation of trial therapy due to adverse events, or AEs, occurred for two patients in the iNO75 arm and one subject in each of the iNO25 and placebo arms.

In February 2016, we announced positive data from the final analysis of our Phase 2 long-term extension clinical trial of INOpulse for PAH, which is Part 2 of our Phase 2 clinical trial of INOpulse for PAH. The data reinforces the results from October 2014 and indicates a sustainability of benefit to PAH patients who received INOpulse 75mcg dose therapy for an average of greater than 12 hours per day and were also treated with LTOT.

Following 16 weeks of blinded therapy in Part 1 of the trial, in Part 2 of the trial, 65 patients were randomized to receive INOpulse doses of either iNO25 or iNO75. The long-term extension analysis was performed after patients had completed between 16 and 32 months of INOpulse treatment, and data from the long-term extension analysis was compared to baseline measurements taken at the beginning of Part 1 of the trial. All patients in the trial were on at least one approved PAH therapy, and most were on two or three PAH therapies.

The long-term extension analysis showed the following:

- Patients on LTOT in the iNO 75 dose treatment arm who remained on INOpulse therapy for at least 12 hours a day had a mean improvement of 55.2 meters as compared to baseline (n=7).

- Patients on LTOT in the iNO 75 dose treatment arm who remained on INOpulse therapy for less than 12 hours a day showed a mean decrease of 18.0 meters as compared to baseline (n=6).

Table of Contents

- Patients on LTOT in the iNO 25 dose treatment arm had a mean decrease of 43.7 meters from baseline (n=12).

For patients in the long-term extension study, no significant safety issues have been found with no reports of methemoglobin elevation and no adjudicated cases of pulmonary rebound. Only two SAEs have been reported as possibly related, with these subjects continuing on iNO therapy.

Pivotal Phase 3 Clinical Trials

After reaching agreement with the FDA and EMA on our Phase 3 protocol, we are moving forward with our Phase 3 development program. In September 2015, the FDA issued a SPA for our Phase 3 PAH program for INOpulse, which will include two confirmatory clinical trials, undertaken either sequentially or in parallel. The first of the two Phase 3 studies has been initiated with the first patient enrolled in June 2016.

The key elements of the planned U.S. and European Union Phase 3 development program are:

- The Phase 3 program will consist of two clinical trials totaling approximately 450 patients; one trial with two treatment arms (iNO 75 and placebo) and one with three treatment arms (iNO 75, iNO 50 and placebo). Each treatment arm will consist of approximately 90 patients. Trial was designed to detect a 40 meter difference in 6MWD assuming a 75 meter standard deviation.

- All patients in the trials will be on LTOT.

- The primary endpoint is improvement in 6MWD compared to placebo after 16 weeks.

- The secondary endpoint is Time to Clinical Worsening (TTCW), with analysis pooled across both trials. Patients will stay on therapy until the last patient visit measuring 6MWD.

- Each trial will have a run-in period of two weeks to ensure compliance. Patients who do not stay on the therapy for at least 16 hours a day during this period will be replaced.

We plan to have our Data Monitoring Committee conduct an un-blinded interim analysis on the first trial after approximately half of the subjects have completed a total of 18 weeks to assess for efficacy, futility and potential sample size reassessment.

INOpulse for PH-COPD

We are developing INOpulse for PH-COPD to address a significant unmet medical need that we believe is often overlooked in everyday clinical practice because of the lack of available therapy. PH is more prevalent among those COPD patients who have advanced loss of respiratory function and low peripheral blood oxygen levels requiring treatment with LTOT. The co-morbidity of PH in these patients leads to cardiovascular complications from the added strain on the right ventricle of the heart. Current drug therapies for COPD are targeted to relieve the symptoms and complications of the respiratory component of the disease. Unlike these therapies, INOpulse is directed at treating the cardiovascular complications of PH-COPD. We believe PH-COPD patients on LTOT who are at risk for cardiovascular complications could benefit from use of INOpulse in addition to any respiratory benefits that result from their existing treatments.

Disease Background and Market Opportunity

COPD is a progressive disease caused by chronic inflammation and destruction of the airways and lung tissue. While COPD is primarily a respiratory disease, over time, as the disease progresses, the chronic pulmonary restrictions and resulting deprivation of adequate oxygen, or hypoxia, can contribute to vasoconstriction in the pulmonary arterial bed. In addition, COPD patients can have deficiency in endogenous nitric oxide production in their lungs, which can worsen vasoconstriction. This pulmonary vasoconstriction puts pressure on the right side of the heart, making it less able to cope with stressors and potentially leading to progressive cardiac dilation, heart

Table of Contents

failure and death. This cardiovascular component of COPD is, we believe, often overlooked despite pulmonologists' general awareness of the problem, in part because there are no specific therapies for the condition in these patients. While it is widely believed that the cardiovascular complications of COPD occur only in the advanced stage of the disease as a consequence of chronic hypoxemia, recent findings demonstrate an earlier involvement of the cardiovascular system in this disease.

In 2010, Datamonitor estimated that approximately 12 million patients in the United States were being treated for COPD and that over 1.4 million of these patients were being treated with LTOT. Based on academic studies, we estimate that 50% of COPD patients on LTOT in the United States have PH. Even though the degree of PH in these patients is milder than in PAH patients, data published in literature suggests that even small elevations in mean pulmonary artery pressure in patients with advanced COPD can impact hospitalization, patient-assessed functional outcomes and mortality. PH is a well-known predictor of increased morbidity and mortality in COPD patients and is associated with poor quality of life, worse clinical outcomes and shorter survival time. Based on a long-term study completed in 1992 and published in 1995, PH-COPD patients had a four-year survival rate of approximately 50%. By contrast, in this same long-term study, COPD patients with similar pulmonary functions, but without PH, had a four-year survival rate of 80%.

The overall COPD market in the United States was estimated to be approximately $32 billion in 2010 with a compounded annual growth rate of approximately 4%. We expect INOpulse for PH-COPD, if approved, would be a treated as a specialty drug. Specialty drugs are typically high-cost medications, often ranging in price in the United States from approximately $15,000 to $50,000 per patient per year, used to treat rare or complex conditions, requiring close clinical management, special handling and distribution through specialty pharmacies.

Scientific Rationale for Use of INOpulse for PH-COPD

The mechanism of action of inhaled nitric oxide in vasodilation at the alveolar smooth muscle in PH-COPD is similar to its action in PAH. Like endogenous pulmonary nitric oxide, inhaled nitric oxide works by selectively relaxing lung vascular smooth muscles, causing dilation of pulmonary blood vessels and consequently increased pulmonary blood flow. This reduces the elevated pulmonary artery pressure in patients with PH-COPD.

PH-COPD patients generally have hypoxemia as a result of deteriorating lung function, which can be treated with supplemental oxygen therapy. However, these patients are not treated with currently approved PAH-specific drugs because these drugs can worsen hypoxemia. This worsening can occur when these drugs, which are systemically bioavailable, cause indiscriminate pulmonary vasodilation, even in poorly ventilated alveoli, resulting in lower average blood oxygenation levels. We believe that pulsed nitric oxide, as a locally active selective pulmonary vasodilator, can avoid the indiscriminate vasodilation associated with drugs that are systemically bioavailable. The INOpulse technology, by targeting the delivery of the pulse to the well ventilated alveoli, has the potential to drop

pulmonary arterial pressure while avoiding the lowering of blood oxygen levels.

The targeted delivery of inhaled nitric oxide to specific alveoli is important because early trials with continuous-flow inhaled nitric oxide reduced pulmonary arterial pressure in PH-COPD patients but also resulted in lowering of blood oxygen levels. It was postulated that this unwanted effect might be avoided by administering nitric oxide as a brief pulse at the beginning of each breath because well-ventilated alveoli open faster, and a brief early pulse would only reach these alveoli. As early as 1997, this concept was demonstrated by testing inhaled nitric oxide in PH-COPD patients during exercise, which allowed the dose to mimic pulse dosing. Recently, data from a computational fluid-flow modeling study we conducted, using high resolution computed tomography scans and computer simulations, supported this hypothesis that early pulsed delivery of nitric oxide could be directed specifically to the well-ventilated alveoli.

Clinical Development Program

INOpulse for PH-COPD is designated as a drug-device combination by the FDA and is being reviewed by the Division of Cardiovascular and Renal Products in the Center for Drug Evaluation and Research with consultation from the Division of Pulmonary, Allergy, and Rheumatology Products and the Center for Devices and Radiological Health. In our IND for PH-COPD, we referenced all of the information in our IND for PAH. The data referenced in our IND, as well as the years of use of the marketed product, demonstrate that nitric oxide is well tolerated. The FDA has agreed that the IND package is adequate for supporting Phase 2 clinical development of

Table of Contents

INOpulse for PH-COPD. The FDA also agreed that no additional pre-clinical studies are needed to support product approval.

We completed a randomized, placebo-controlled, double-blind, dose-confirmation Phase 2 clinical trial of INOpulse for PH-COPD in July 2014. We have received results from this trial, and have initiated further Phase 2 testing to demonstrate the potential benefit on exercise capacity. In September 2015, an oral presentation of late-breaking data from a clinical trial sponsored by us was presented at the European Respiratory Society International Congress 2015 in Amsterdam. The data showed that INOpulse improved vasodilation in patients with PH-COPD. Building upon this and other work we have done over recent quarters, we have initiated additional Phase 2 testing for the use of the INOpulse device for PH-COPD patients to evaluate the potential benefit of chronic use on exercise capacity, with the first patient enrolled in October 2016.

The initiated Phase 2 study in PH-COPD is an open-label study looking at both vasodilation and exercise capacity on 10 COPD patients with pulmonary hypertension who are also on long-term oxygen therapy. The key elements of the study are:

- iNO 30 mcg/kg IBW/hr dose for 4 weeks with a follow-up visit 2 weeks after discontinuation
- All patients in the trials will be on LTOT.
- The primary endpoint is vasodilation in pulmonary arteries measured by high resolution CT scanning (HRCT)
- Key secondary endpoint is 6MWD
- HRCT will be done at baseline and end of 4 weeks with 6MWT performed at baseline, 2 weeks, 4 weeks and 6 weeks (2 weeks after discontinuation of therapy)

INOpulse for PH-IPF

We are also developing INOpulse for the treatment of PH-IPF. IPF is a progressive disease of unknown etiology associated with growth of fibrotic tissue in the lungs causing hypoxemia, dyspnea, fatigue and cough. The median survival is only 2-3 years. Based on academic studies, we estimate the prevalence of IPF in the United States at approximately 90,000 patients, with 20-40% suffering from pulmonary hypertension. PH with IPF increases mortality. The presence of PH correlates most closely with the need for oxygen therapy. The two therapies that are currently

approved for IPF, nintedanib and perfinidone cost approximately $100,000 per year.

iNO may improve outcomes in PH-IPF by both improving V/Q matching with increases in arterial oxygenation and by lowering pulmonary artery pressures. It has been shown (Yoshida et al) that inhalation of NO significantly reduced the mean pulmonary arterial pressure and the pulmonary vascular resistance as compared with room air alone. However the arterial oxygen tension (PaO2) did not improve. The combined inhalation of NO and oxygen produced a significant decrease of pulmonary arterial pressure ($p<0.01$) as well as an improvement ($p<0.05$) in PaO2 as compared to oxygen alone. These findings support the potential for the combined use of nitric oxide and oxygen for treating idiopathic pulmonary fibrosis patients with pulmonary hypertension.

Clinical Development Program

A Phase 2 study in PH-IPF has been initiated looking at both vasodilation and exercise capacity on 4 IPF patients with pulmonary hypertension who are also on long-term oxygen therapy. The study is made up of a double blind, randomized, placebo controlled, acute phase to visualize vasodilation with high resolution computed

Table of Contents

tomography (HRCT). This is followed by an open label chronic phase (4 weeks on iNO 75 then 2 week withdrawal period) to assess 6MWD.

INOpulse for Other Pulmonary Hypertension Conditions

PH disease is often classified according to the WHO classification system which groups patients with PH according to the underlying etiologies, or causes, of the PH. In this system, PAH is defined as Group 1 and PH-COPD is classified under Group 3, PH due to lung disease and/or hypoxemia. We believe the mechanism of action of inhaled nitric oxide as a pulmonary vasodilator, and thus INOpulse, can be effective in treating PH related to other conditions, including PH associated with IPF, CTEPH, PH associated with sarcoidosis and PH associated with pulmonary edema from high altitude sickness.

While there are two recently approved treatments for IPF, there are currently no approved therapies for PH-IPF. In 2013, riociguat (Adempas) was the first drug therapy approved for treating CTEPH, although other PAH medications are sometimes used to treat this condition. Patients with sarcoidosis are often treated with steroids or other anti-inflammatory medications, however, there are no therapies approved to treat the PH associated with this disease. Pulmonary edema from high altitude sickness is typically treated with oxygen therapy, however, there are no current treatments for PH associated with this disease.

Our current license from Ikaria covers the development of the Bellerophon indications as noted above.

Relationship with Ikaria after the Spin-Out

The development of our programs was initiated under the leadership of our scientific and development team while at Ikaria. Ikaria's lead product, INOmax, is an inhaled nitric oxide product used for treatment of persistent PH of the newborn. Our understanding of the medical applications of nitric oxide and associated delivery devices, as well as our innovative approach to the pulsed delivery of nitric oxide, originated at Ikaria.

In October 2013, Ikaria completed an internal reorganization of certain assets and subsidiaries, in which it transferred to us exclusive worldwide royalty-free rights to develop and commercialize pulsed nitric oxide in PAH, PH-COPD and PH-IPF. In November 2015, we entered into an amendment to our exclusive cross-license, technology transfer and regulatory matters agreement with Ikaria that included a royalty equal to 3% of net sales of any commercial products for PAH. Following the internal reorganization, in February 2014, Ikaria distributed all of our then

outstanding units to its stockholders through the payment of a special dividend on a pro rata basis based on each stockholder's ownership of Ikaria capital stock. We refer to Ikaria's distribution of our then outstanding units to its stockholders as the Spin-Out.

Shortly after the Spin-Out, Ikaria was acquired by entities affiliated with Madison Dearborn Partners. On April 16, 2015, Mallinckrodt plc, or Mallinckrodt, announced that it had completed its acquisition of Ikaria.

In connection with the Spin-Out, we entered into several agreements with Ikaria providing for, among other things, the provision of transition services, the cross license of certain intellectual property, commitments not to compete, the manufacture and supply of the INOpulse drug and device and certain employee matters.

Table of Contents

Transition Services Agreement and 2015 Services Agreement

In February 2014 and July 2015, we entered into a transition services agreement and an amendment to the transition services agreement, respectively, with Ikaria, which we refer to as the TSA. Pursuant to the terms and conditions of the TSA, Ikaria had agreed to use commercially reasonable efforts to provide certain services to us until February 2016. In exchange for the services provided by Ikaria pursuant to the TSA, we paid to Ikaria a service fee in the amount of $772,000 per month and reimbursed Ikaria for any out of pocket expenses, any taxes imposed on Ikaria in connection with the provision of services under the TSA. The termination of these services was accelerated to September 30, 2015 as part of the amendment to the agreement entered in July 2015.

Under our additional services agreement with Ikaria, or the 2015 Services Agreement, which became effective on January 1, 2015, Ikaria provided to us certain information technology and device servicing services. In exchange for the services provided by Ikaria pursuant to the 2015 Services Agreement, we paid to Ikaria fees that totaled, in the aggregate, approximately $0.2 million. We also received payments of $1.7 million from Ikaria in connection with the 2015 Services Agreement for using commercially reasonable efforts to provide certain services to Ikaria, including services related to regulatory matters, drug and device safety, clinical operations, biometrics and scientific affairs. In July 2015, we entered into an amendment to the 2015 Services Agreement advancing the termination date from February 8, 2016 to September 30, 2015.

Exclusive Cross-License, Technology Transfer and Regulatory Matters Agreement

In February 2014, we entered into an exclusive cross-license, technology transfer and regulatory matters agreement with Ikaria. Pursuant to the terms of the license agreement, Ikaria granted to us a fully paid-up, non-royalty bearing, exclusive license under specified intellectual property rights controlled by Ikaria to engage in the development, manufacture and commercialization of nitric oxide, devices to deliver nitric oxide and related services for or in connection with out-patient, chronic treatment of patients with PAH, PH-COPD or PH-IPF. On July 27, 2015, we entered into an amendment to the license agreement to expand the scope of our license to allow us to develop our INOpulse program for the treatment of three additional indications: CTEPH, PH associated with sarcoidosis and PH associated with pulmonary edema from high altitude sickness. Subject to the terms set forth therein, the amendment to the license agreement also provides that the Company will pay Ikaria a royalty equal to 5% of net sales of any commercialized products for the three additional indications. In November 2015, we entered into an amendment to our exclusive cross-license, technology transfer and regulatory matters agreement with Ikaria that included a royalty equal to 3% of net sales of any commercial products for PAH.

We have granted to Ikaria a fully paid-up, non-royalty-bearing, exclusive license under specified intellectual property rights that we control to engage in the development, manufacture and commercialization of products and services for or used in connection with the diagnosis, prevention or treatment, whether in- or out-patient, of certain conditions and

diseases other than the Bellerophon indications and for the use of nitric oxide to treat or prevent conditions that are primarily managed in the hospital, which we refer to collectively as the Ikaria nitric oxide business.

We have agreed that, during the term of the license agreement, we will not, without the prior written consent of Ikaria, grant a sublicense under any of the intellectual property licensed to us under the license agreement to any of our affiliates or any third party, in either case that directly or indirectly competes with the Ikaria nitric oxide business. We have also agreed that we will include certain restrictions in our agreements with customers of our products to ensure that such products will only be used for the Bellerophon indications.

The license agreement will expire on a product-by-product basis for products for a specific Bellerophon indication at such time as we are no longer developing or commercializing any product for such indication. The license agreement may be terminated by either party in the event an act or order of a court or governmental authority prohibits either party from substantially performing under the license agreement. Either party may also terminate the license agreement in the event of an uncured material breach by the other party or in the event the other party is insolvent or in bankruptcy proceedings. Ikaria may also terminate the license agreement if we or any of our affiliates breach the agreements not to compete described below, or if we or any successor to our rights under the license agreement markets a generic nitric oxide product that is competitive with INOmax. Under certain circumstances, if the license agreement is terminated, the licenses granted to Ikaria by us will survive such termination.

Table of Contents

Ikaria retains the right to develop and commercialize inhaled nitric oxide products, including pulsed products, in all indications other than the Bellerophon indications.

Agreements Not to Compete

In September 2013, October 2013 and February 2014, we and each of our subsidiaries entered into an agreement not to compete with Ikaria, each of which was amended in July 2015. We refer to these agreements collectively as the agreements not to compete. Pursuant to the agreements not to compete, as amended, we and each of our subsidiaries agreed not to engage, anywhere in the world, in any manner, directly or indirectly, until the earlier of five years after the effective date of such agreement not to compete, as amended, or the date on which Ikaria and all of its subsidiaries are no longer engaged in such business, in:

- the development, manufacture, commercialization, promotion, sale, import, export, servicing, repair, training, storage, distribution, transportation, licensing or other handling or disposition of any product or service (including, without limitation, any product or service that utilizes, contains or includes nitric oxide for inhalation, a device intended to deliver nitric oxide or a service that delivers or supports the delivery of nitric oxide), bundled or unbundled, for or used in connection with (a) the diagnosis, prevention or treatment, in both adult and/or pediatric populations, and whether in- or out-patient, of: (i) hypoxic respiratory failure associated with pulmonary hypertension, (ii) pulmonary hypertensive episodes and right heart failure associated with cardiovascular surgery, (iii) bronchopulmonary dysplasia, (iv) the management of ventilation-perfusion mismatch in acute lung injury, (v) the management of ventilation-perfusion mismatch in acute respiratory distress syndrome, (vi) the management of pulmonary hypertension episodes and right heart failure in congestive heart failure, (vii) the management of pulmonary hypertension episodes and right heart failure in pulmonary or cardiac surgery, (viii) the management of pulmonary hypertension episodes and right heart failure in organ transplant, (ix) sickle cell vaso-occlusive crisis, (x) hypoxia associated with pneumonia or (xi) ischemia-reperfusion injury or (b) the use of nitric oxide to treat or prevent conditions that are primarily managed in the hospital; or

- any and all development, manufacture, commercialization, promotion, sale, import, export, storage, distribution, transportation, licensing, or other handling or disposition of any terlipressin or any other product within the pressin family, (a) intended to treat (i) hepatorenal syndrome in any form, (ii) bleeding esophageal varices or (iii) septic shock or (b) for or in connection with the management of low blood pressure.

The agreements not to compete expressly exclude the Bellerophon indications.

In February 2014, we also entered into drug and device clinical supply agreements and an employee matters agreement with Ikaria. In November 2015, we entered into an amendment to the drug supply agreement. See “Manufacturing” below for a description of the drug and device clinical supply agreements and “Certain Relationships

and Related Person Transactions-Relationship with Ikaria" for a description of the employee matters agreement.

Manufacturing

INOpulse Drug Product

In February 2014, we and a subsidiary of Ikaria entered into a drug supply agreement which was subsequently amended in November 2015. Under this agreement, Ikaria has agreed to use commercially reasonable efforts to supply inhaled nitric oxide for us in our clinical trials, and we have agreed to purchase our clinical supply of inhaled nitric oxide from Ikaria. We have also granted Ikaria a right of first negotiation in the event that we desire to enter into a commercial supply agreement with a third party for supply of nitric oxide for inhalation. The drug supply agreement will expire on a product-by-product basis on the date we discontinue clinical development of such product. In addition, either party may terminate the drug supply agreement in the event of an uncured material breach by the other party.

Table of Contents

Ikaria manufactures pharmaceutical-grade nitric oxide at its facility in Port Allen, Louisiana. This facility, which we believe is operated in compliance with current Good Manufacturing Practices, or cGMP, is the only FDA-approved site for manufacturing medical nitric oxide in the world.

To support business outside of the United States, the Port Allen manufacturing facility has also successfully passed inspections by the EMA, Health Canada; the Pharmaceutical and Medical Devices Agency, or PMDA, of Japan, and the Korean FDA, or KFDA. The EMA, the Health Protection Branch of Health Canada, PMDA and KFDA operate in a similar fashion to the FDA in that each requires submission of a dossier containing substantial evidence of safety and effectiveness prior to approval. These agencies' monitoring of safety in a post-marketing setting also is similar to that of the FDA.

The filling process has been developed by Ikaria as a high-throughput batch fill process that leverages several technologies that Ikaria has developed, and we have licensed, to fill the cartridge (containers) at a higher pressure and purity.

This manufacturing system is designed to be modular and can be expanded as needed. The current installed capacity within the Port Allen plant is sufficient to support our INOpulse clinical program as currently planned. In addition, the plant has the capacity to expand to meet additional demand. We have a license from Ikaria to use this fill process technology to work with additional companies, as needed, to produce the final cartridge. Commercial supply manufacturing can be supported with additional units installed at the Port Allen site or other regional locations, by Ikaria or other manufacturers, as determined by distribution requirements. For our clinical trials, Ikaria can supply and ship product from the Port Allen site and the current cartridges have a shelf life of at least two years. We are testing the finished product to potentially establish a shelf life of up to three years.

INOpulse Drug Delivery Systems

In February 2015, we entered into an agreement with Flextronics Medical Sales and Marketing Ltd., a subsidiary of Flextronics International Ltd., or Flextronics, to manufacture and service the INOpulse device that we will use in future clinical trials of INOpulse for PAH and INOpulse for PH-COPD and PH-IPF.

PAH patients have the potential for rebound PH, which is a sudden and serious increase in pulmonary arterial pressure that results from therapy withdrawal. However, in the Phase 2 trial, all patients were tested for rebound PH and we found no adjudicated cases of rebound PH with this testing. Subjects in our PAH trials are all on at least one background specific PAH therapy, the majority being on two or more PAH therapies. These background therapies likely protect against rebound. Though the likelihood of rebound PH is very low, all patients with PAH are provided

with a backup system.

Competition

The biotechnology and pharmaceutical industries are highly competitive. There are many pharmaceutical companies, biotechnology companies, public and private universities and research organizations actively engaged in the research and development of products that may be similar to our products. In addition, other companies are increasingly looking at cardiopulmonary indications as a potential opportunity. It is possible that the number of companies seeking to develop products and therapies for the treatment of unmet needs in our target markets will increase.

Our competitors, either alone or with their strategic partners, may have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Accordingly, our competitors may be more successful than we may be in obtaining approval for therapies and achieving widespread market acceptance. We anticipate that we will face intense and increasing competition as new drugs and advanced technologies become available.

Currently, there are 14 drugs approved for the treatment of PAH, within the following categories: prostacyclin and prostacyclin analogs (including Flolan (epoprostenol), which is marketed by GlaxoSmithKline, Tyvaso (treprostinil), Orenitram (treprostinil) and Remodulin (treprostinil), which are marketed by United Therapeutics Corporation, Ventavis (iloprost) and Veletri (epoprostenol), which are marketed by Actelion

Table of Contents

Pharmaceuticals US, Inc., or Actelion, and Beraprost (which is a generic available in Asian markets), phosphodiesterase type-5 inhibitors (including Adcirca (tadalafil), which is marketed by United Therapeutics Corporation, and Revatio (sildenafil), which is marketed by Pfizer Inc.), endothelin receptor antagonists (including Letairis (ambrisentan), which is marketed by Gilead Sciences, Inc., and Opsumit (macitentan) and Tracleer (bosentan), which are marketed by Actelion) and a soluble guanylate cyclase stimulator (Adempas (riociguat), which is marketed by Bayer HealthCare Pharmaceuticals Inc.). The most recent addition to the list is Uptravi (selexipag), a selective prostacyclin receptor agonist, which is marketed by Actelion and was approved by the FDA in December 2015.

There are also other treatments for PAH in various phases of development, including other nitric oxide generation and delivery systems such as GeNOsyl™ (being developed by GeNO LLC) and a nebulized formulation of nitrite (being developed by Mast Therapeutics) both in Phase 2 development. Further, Insmed, Inc. is developing an investigational, sustained-release, inhaled treprostinil prodrug and SteadyMed Therapeutics, Inc., or Steady Med, is developing Trevyent™ which delivers treprostinil using SteadyMed's PatchPump technology.

Currently, there are no approved therapies for treating PH-COPD, and the only generally accepted treatments are LTOT, pulmonary rehabilitation and lung transplant, and we are not aware of any therapies for PH-COPD in advanced clinical development.

Patents and Proprietary Rights

We strive to protect the proprietary technologies that we believe are important to our business, including seeking and maintaining patent protection intended to protect, for example, our product candidates, related technologies and/or other aspects of the inventions that are important to our business. Our owned and licensed patents and patent applications cover patentable subject matter from composition of matter, methods of use, devices and device components, critical safety features and design components with respect to INOpulse. However, patent protection is not available for the composition of matter of the active pharmaceutical ingredients in INOpulse since nitric oxide is a naturally occurring molecule.

Actual protection afforded by a patent, which can vary from country to country, depends on the type of patent, the scope of its coverage and the availability of legal remedies in the country. We also rely on trade secrets and careful monitoring of our proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

We plan to continue to expand our intellectual property estate by filing patent applications directed to inventions which provide additional patent protection for our product offering, for instance, device enhancements, safety features and manufacturing processes. Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our patents; maintain our licenses to use intellectual property owned by third parties; preserve the confidentiality of our trade secrets; and operate without infringing the valid and enforceable patents and other proprietary rights of third parties. We also consider know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary positions.

A third party may hold intellectual property, including patent rights that are important or necessary to the development of our programs. 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 obtain a license from these third parties on commercially reasonable terms, or our business could be harmed, possibly materially. For example, if we want to expand the indications for which we could develop and commercialize pulsed nitric oxide beyond the Bellerophon indications, we will need to obtain a license from Ikaria.

The patent positions of therapeutics companies like us are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and patent scope can be reinterpreted by the courts after issuance. Moreover, many jurisdictions permit third parties to challenge issued patents in administrative proceedings which may result in further narrowing or even cancellation of patent claims. Consequently, we do not know whether any of our product

Table of Contents

candidates will be protectable or remain protected by enforceable patents. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors. Any patents that we own or license may be challenged, narrowed, circumvented or invalidated by third parties.

Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months or potentially even longer, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain of the priority of inventions covered by pending patent applications. Moreover, we may have to participate in interference proceedings declared by the U.S. Patent and Trademark Office, or USPTO, to determine priority of inventions for any patent applications filed with the USPTO on or before March 15, 2013. Likewise, derivation proceedings may also be declared for any patent filings filed after March 15, 2013.

The patents and patent applications that relate to our programs are described below.

INOpulse

As of March 10, 2016, we hold exclusive licenses from Ikaria to at least 80 patents and pending patent applications in both the United States and foreign countries including Australia, Brazil, Canada, China, Europe, Hong Kong, India, Indonesia, Israel, Japan, Korea, Mexico, the Philippines, Russia and Singapore. Certain of these issued patents and patent applications, if issued, will expire as late as 2033. These patent rights have been exclusively licensed for the treatment of patients with Bellerophon indications and cover methods of delivery and the drug delivery device, as well as important safety features and the ornamental design of the drug delivery device.

A primary basis for patent exclusivity is based on pending and issued in-licensed patents directed to proprietary methods of administering pulsed inhaled nitric oxide, as well as a device for delivering the same. At least one patent has been issued in the United States as well as Australia, China, Hong Kong, Japan, and Mexico. One patent has been allowed in Europe where the PTO has issued a Notice of Intention to Grant. Patent applications are pending in Australia, Brazil, Canada, China, Europe, Hong Kong, Mexico and the United States. This patent family expires as late as 2027 in the United States and as late as 2026 in the other countries.

Another important basis for patent exclusivity is based on an in-licensed portfolio of patents, directed to novel nasal cannula features that we believe are necessary for the accurate, safe and efficacious administration of pulsed nitric oxide. The patent family consists of two issued U.S. patents and pending applications in the United States as well as Australia, Brazil, Canada, China, Russia, Europe, Israel, India, Japan, Korea and Mexico. Each of these patents and patent applications, if issued, will expire in 2033 in the United States and abroad.

Another in-licensed patent family relates to features of the drug delivery canister necessary for providing drug product for use with our proprietary pulsing drug delivery device. This patent family includes one issued U.S. patent, one issued Japanese patent, one issued Mexican patent, one issued Singaporean patent, one issued Israeli patent, one issued Chinese patent, one issued Indonesian patent, one issued Korean patent, one issued Russian patent, and three issued Australian patents, as well as 14 pending patent applications in the United States, Brazil, Canada, China, Europe, Hong Kong, India, Israel, Japan, Korea, Mexico, the Philippines, Russia and Singapore. These pending applications, if issued, as well as the non-U.S. issued patents will expire in 2029. The issued U.S. patent will expire in 2030.

Several other patent families directed to device and safety features are issued and pending. Furthermore, a design patent covering the ornamental design of the intended commercial device and clinical device has been granted.

In addition, the FDA has granted orphan drug designation to our nitric oxide program for the treatment of PAH, which could result in marketing exclusivity of seven years in the United States should this be the first NDA approved for inhaled nitric oxide in this indication. The active ingredient, nitric oxide, was previously approved by the FDA as a drug in a separate clinical application. Accordingly, any related patent rights will not be eligible for a patent term extension under relevant provisions of the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act.

Table of Contents

Patent Term

The base term of a U.S. patent is 20 years from the filing date of the earliest-filed non-provisional patent application from which the patent claims priority. The term of a U.S. patent can be lengthened by patent term adjustment, which compensates the owner of the patent for administrative delays at the USPTO. In some cases, the term of a U.S. patent is shortened by a terminal disclaimer that reduces its term to that of an earlier-expiring patent.

The term of a U.S. patent may be eligible for patent term extension under the Hatch-Waxman Act to account for at least some of the time the drug or device is under development and regulatory review after the patent is granted. With regard to a drug or device for which FDA approval is the first permitted marketing of the active ingredient, the Hatch-Waxman Act allows for extension of the term of one U.S. patent. Thus, patent term extension is not available for INOpulse since the active moiety is nitric oxide, which is already subject to an approved NDA. The extended patent term cannot exceed the shorter of five years beyond the non-extended expiration of the patent or 14 years from the date of the FDA approval of the drug or device. Some foreign jurisdictions have analogous patent term extension provisions that allow for extension of the term of a patent that covers a device approved by the applicable foreign regulatory agency.

Trade Secrets

In addition to patents, we rely on trade secrets and know-how to develop and maintain our competitive position. We typically rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. For example, elements of the manufacture of our products are based on trade secrets and know-how that are not publicly disclosed. We protect trade secrets and know-how by establishing confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and commercial partners. These agreements provide that all confidential information developed or made known during the course of an individual or entity's relationship with us must be kept confidential during and after the relationship. These agreements also provide that all inventions resulting from work performed for us or relating to our business and conceived or completed during the period of employment or assignment, as applicable, shall be our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary technology by third parties.

Trademarks

We also seek trademark protection where available and when appropriate. The symbol ™ indicates a common law trademark. Other service marks, trademarks and trade names appearing in this prospectus are the property of their

respective owners.

Government Regulation

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

Review and Approval of Drugs in the United States

In the United States, the FDA regulates drugs under the Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of

Table of Contents

administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or other governmental entities.

Our product candidates must be approved by the FDA before they may be legally marketed in the United States. An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of pre-clinical laboratory tests, animal studies and formulation studies in compliance with applicable FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an investigational new drug application, or IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, at each clinical site before a clinical trial may be initiated at that site;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;
- preparation and submission to the FDA of a new drug application, or NDA;
- review of the product by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with cGMP requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- payment of user fees and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including Risk Evaluation and Mitigation Strategies, or REMS, and post-approval studies required by the FDA.

Pre-Clinical Studies

Pre-clinical studies include laboratory evaluation of the purity and stability of the manufactured drug substance or active pharmaceutical ingredient and the formulated drug or drug product, as well as *in vitro* and animal studies to assess the toxicity, safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of pre-clinical and other non-clinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the pre-clinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND.

Companies usually must complete some long-term pre-clinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the drug in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

Table of Contents

Human Clinical Studies in Support of an NDA

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

In addition, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations.

A sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA or IND so long as the clinical trial is conducted in compliance with GCP, and the FDA is able to validate the data from the trial through an onsite inspection if the agency deems it necessary.

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

- Phase 1: The drug is initially introduced into a small number of healthy human subjects or patients with the target disease (e.g., cancer) or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.

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

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Phase 3: Phase 3 clinical trials are commonly referred to as “pivotal” studies, which typically denotes a clinical trial which is intended to present the data that the FDA or other relevant regulatory agency will use to determine whether or not to approve a drug. In Phase 3 clinical trials, the drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if SAEs occur. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB’s requirements or if the drug has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted. In addition, the sponsor of a clinical trial must register with the National Institutes of Health, or NIH, and list information about the trial on NIH's clinicaltrials.gov website.

Table of Contents

Section 505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical trials that must contain substantial evidence of the safety and efficacy of the proposed new product. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the applicant to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the applicant for approval of the application "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Thus, Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain pre-clinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

Submission of an NDA to the FDA

Assuming successful completion of required clinical trials and other requirements, the results of the non-clinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to an application user fee, currently exceeding $2.1 million, and the sponsor of an approved NDA is also subject to annual product and establishment fees, currently exceeding $104,000 per product and $554,000 per establishment. These fees are typically increased annually.

The FDA conducts a preliminary review of an NDA within 60 days of its receipt and informs the sponsor by the 74th day after the FDA's receipt of the submission whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs. Most such

applications are meant to be reviewed within ten months from the date of filing, and most applications for "priority review" products are meant to be reviewed within six months of filing. The review process may be extended by the FDA for various reasons, including for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

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

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

Table of Contents

Special Protocol Assessment

A sponsor of an IND may request that the FDA evaluate within 45 days certain protocols and issues relating to the protocols to assess whether they are adequate to meet scientific and regulatory requirements identified by the sponsor. Such special protocol assessments, or SPAs, may be requested for clinical protocols for Phase 3 trials whose data will form the primary basis for an efficacy claim if the trials had been the subject of discussion at an end-of-Phase 2/pre-Phase 3 meeting with the FDA. If the sponsor and the FDA reach a written agreement regarding the protocol, the SPAs will be considered binding on the FDA and will not be changed unless the sponsor fails to follow the agreed-upon protocol, data supporting the request are found to be false or incomplete, or the FDA determines that a substantial scientific issue essential to determining the safety or effectiveness of the drug was identified after the testing began. Even if a SPA is agreed to, approval of the NDA is not guaranteed since a final determination that an agreed-upon protocol satisfies a specific objective, such as the demonstration of efficacy, or supports an approval decision, will be based on a complete review of all the data in the NDA.

Accelerated Approval Pathway

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

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

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the

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

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the

Table of Contents

type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions which can materially affect the potential market and profitability of the product. In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product.

The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Requirements

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

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP and other requirements. Changes to the

manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

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

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

Table of Contents

- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;

- product seizure or detention, or refusal to permit the import or export of products; or

- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. In support of such applications, a generic manufacturer may rely on the pre-clinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference listed drug, or RLD.

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

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

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. In cases where such exclusivity has been granted, an ANDA may not be submitted to the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication.

Table of Contents

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant submits its application to the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicate that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

If the ANDA applicant or 505(b)(2) applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the ANDA applicant.

Orphan Designation and Exclusivity

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

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation, the product will be entitled to orphan product exclusivity. Orphan product exclusivity means that FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances. Competitors may receive approval of different products for the indication for which the orphan product has exclusivity and may obtain approval for the same product but for a different indication. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003, a NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant

Table of Contents

pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the Food and Drug Administration Safety and Innovation Act, or FDASIA, in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

Patent Term Restoration and Extension

A patent claiming a new drug product or medical device may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted on a patent covering a new drug product is typically one-half the time between the date a clinical investigation on human beings is begun and the submission date of an application for premarket approval of the product, plus the time between the submission date of an application for approval of the product and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Review and Approval of Medical Devices in the United States

Medical devices in the United States are strictly regulated by the FDA. Under the FDCA a medical device is defined as an instrument, apparatus, implement, machine, contrivance, implant, *in vitro* reagent, or other similar or related article, including a component, part or accessory which is, among other things: intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals; or intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes. This definition provides a clear distinction between a medical device and other FDA regulated products such as drugs. If the primary intended use of the product is achieved through chemical action or by being metabolized by the body, the product is usually a drug. If not, it is generally a medical device.

Unless an exemption applies, a new medical device may not be marketed in the United States unless and until it has been cleared through the 510(k) premarket notification process, or 510(k), or approved by the FDA pursuant to a premarket approval application, or PMA. The information that must be submitted to the FDA in order to obtain clearance or approval to market a new medical device varies depending on how the medical device is classified by the FDA. Medical devices are classified into one of three classes on the basis of the controls deemed by the FDA to be necessary to reasonably ensure their safety and effectiveness.

Table of Contents

Class I devices are those low risk devices for which reasonable assurance of safety and effectiveness can be provided by adherence to the FDA's general controls for medical devices, which include applicable portions of the FDA's Quality System Regulation, or QSR, facility registration and product listing, reporting of adverse medical events and malfunctions and appropriate, truthful and non-misleading labeling, advertising and promotional materials. Many Class I devices are exempt from premarket regulation; however, some Class I devices require premarket clearance by the FDA through the 510(k) premarket notification process.

Class II devices are moderate risk devices and are subject to the FDA's general controls, and any other special controls, such as performance standards, post-market surveillance, and FDA guidelines, deemed necessary by the FDA to provide reasonable assurance of the devices' safety and effectiveness. Premarket review and clearance by the FDA for Class II devices are accomplished through the 510(k) premarket notification procedure, although some Class II devices are exempt from the 510(k) requirements. Premarket notifications are subject to user fees, unless a specific exemption applies.

Class III devices are deemed by the FDA to pose the greatest risk, such as those for which reasonable assurance of the device's safety and effectiveness cannot be assured solely by the general controls and special controls described above and that are life-sustaining or life-supporting. A PMA application must provide valid scientific evidence, typically extensive pre-clinical and clinical trial data and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications (and supplemental PMA applications) are subject to significantly higher user fees than are 510(k) premarket notifications.

Post-Marketing Restrictions and Enforcement

After a device is placed on the market, numerous regulatory requirements apply. These include, but are not limited to:

- submitting and updating establishment registration and device listings with the FDA;

- compliance with the QSR, which requires manufacturers to follow stringent design, testing, control, documentation, record maintenance, including maintenance of complaint and related investigation files, and other quality assurance controls during the manufacturing process;

- unannounced routine or for-cause device inspections by the FDA, which may include our suppliers' facilities; and

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labeling regulations, which prohibit the promotion of products for uncleared or unapproved or "off-label" uses and impose other restrictions on labeling; post-approval restrictions or conditions, including requirements to conduct post-market surveillance studies to establish continued safety data or tracking products through the chain of distribution to the patient level.

Under the FDA medical device reporting, or MDR, regulations, medical device manufacturers are required to report to the FDA information that a device has or may have caused or contributed to a death or serious injury or has malfunctioned in a way that would likely cause or contribute to death or serious injury if the malfunction of the device or a similar device of such manufacturer were to recur. The decision to file an MDR involves a judgment by the manufacturer. If the FDA disagrees with the manufacturer's determination, the FDA can take enforcement action.

Additionally, the FDA has the authority to require the recall of commercialized products in the event of material deficiencies or defects in design or manufacture. The authority to require a recall must be based on an FDA finding that there is reasonable probability that the device would cause serious adverse health consequences or death. Manufacturers may, under their own initiative, recall a product if any material deficiency in a device is found. The FDA requires that certain classifications of recalls be reported to the FDA within ten working days after the recall is initiated.

Table of Contents

The failure to comply with applicable regulatory requirements can result in enforcement action by the FDA, which may include any of the following sanctions:

- warning letters, fines, injunctions or civil penalties;
- recalls, detentions or seizures of products;
- operating restrictions;
- delays in the introduction of products into the market;
- total or partial suspension of production;
- delay or refusal of the FDA or other regulators to grant 510(k) clearance or PMA approvals of new products;
- withdrawals of 510(k) clearance or PMA approvals; or
- in the most serious cases, criminal prosecution.

To ensure compliance with regulatory requirements, medical device manufacturers are subject to market surveillance and periodic, pre-scheduled and unannounced inspections by the FDA, and these inspections may include the manufacturing facilities of subcontractors.

Review and Approval of Combination Products in the United States

Certain products may be comprised of components that would normally be regulated under different types of regulatory authorities, and frequently by different Centers at the FDA. These products are known as combination products. Specifically, under regulations issued by the FDA, a combination product may be:

- a product comprised of two or more regulated components that are physically, chemically, or otherwise combined or mixed and produced as a single entity;

- two or more separate products packaged together in a single package or as a unit and comprised of drug and device products;

- a drug or device packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug or device where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the approved product would need to be changed, e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose; or

- any investigational drug or device packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect.

Under the FDCA, the FDA assigns primary jurisdiction to a lead center at the FDA for review of a combination product. That determination is based on the “primary mode of action” of the combination product. Thus, if the primary mode of action of a device-drug combination product is attributable to the drug product, the Center for Drug Evaluation and Research would have primary jurisdiction for the combination product. The FDA's Office of Combination Products addresses issues related to combination products and is intended to provide more certainty to the regulatory review process. That office serves as a focal point for combination product issues for agency reviewers and industry. It is also responsible for developing guidance and regulations to clarify the

Table of Contents

regulation of combination products, and for assignment of the FDA center that has primary jurisdiction for review of combination products where the jurisdiction is unclear or in dispute.

Review and Approval of Drug Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of drug products. Whether or not it obtains FDA approval for a product, the company will have to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Pursuant to the European Clinical Trials Directive, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, an applicant must submit a clinical trial authorization, or CTA, and obtain approval from the competent national authority of a European Union member state in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial after a competent ethics committee has issued a favorable opinion. A CTA must be accompanied by an investigational medicinal product dossier with supporting information prescribed by the European Clinical Trials Directive and corresponding national laws of the member states and further detailed in applicable guidance documents.

To obtain marketing approval of a drug under European Union regulatory systems, an applicant must submit a marketing authorization application, or MAA, either under a centralized or decentralized procedure.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all European Union member states. The centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established at the EMA, is responsible for conducting the initial assessment of a drug. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. In this circumstance, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure is available to applicants who wish to market a product in various European Union member states where such product has not received marketing approval in any European Union member states before. The decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state designated by the applicant, known as the reference member state. Under this procedure, an applicant submits an application based on identical dossiers and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment report and drafts of the related materials within 210 days after receipt of a valid application. Within 90 days of

Table of Contents

receiving the reference member state's assessment report and related materials, each concerned member state must decide whether to approve the assessment report and related materials.

If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may eventually be referred to the European Commission, whose decision is binding on all member states.

Review and Approval of Medical Devices in the European Union

The European Union has adopted numerous directives and standards regulating, among other things, the design, manufacture, clinical trials, labeling, approval and adverse event reporting for medical devices. In the European Union, medical devices must comply with the Essential Requirements in Annex I to the EU Medical Devices Directive (Council Directive 93/42/EEC), or the Essential Requirements. Compliance with these requirements is a prerequisite to be able to affix the CE mark of conformity to medical devices, without which they cannot be marketed or sold in the European Economic Area, or EEA, comprised of the European Union member states plus Norway, Iceland, and Liechtenstein. Actual implementation of these directives, however, may vary on a country-by-country basis.

To demonstrate compliance with the Essential Requirements a manufacturer must undergo a conformity assessment procedure, which varies according to the type of medical device and its classification. Except for low risk medical devices, where the manufacturer can issue a CE Declaration of Conformity based on a self-assessment of the conformity of its products with the Essential Requirements, a conformity assessment procedure requires the intervention of a third-party organization designated by competent authorities of a European Union country to conduct conformity assessments, or a Notified Body. Notified Bodies are independent testing houses, laboratories, or product certifiers typically based within the European Union and authorized by the European member states to perform the required conformity assessment tasks, such as quality system audits and device compliance testing. The Notified Body would typically audit and examine the product's Technical File and the quality system for the manufacture, design and final inspection of the product before issuing a CE Certificate of Conformity demonstrating compliance with the relevant Essential Requirements.

Medical device manufacturers must carry out a clinical evaluation of their medical devices to demonstrate conformity with the relevant Essential Requirements. This clinical evaluation is part of the product's Technical File. A clinical evaluation includes an assessment of whether a medical device's performance is in accordance with its intended use, and that the known and foreseeable risks linked to the use of the device under normal conditions are minimized and acceptable when weighed against the benefits of its intended purpose. The clinical evaluation conducted by the manufacturer must also address any clinical claims, the adequacy of the device labeling and information (particularly claims, contraindications, precautions and warnings) and the suitability of related Instructions for Use. This

assessment must be based on clinical data, which can be obtained from clinical studies conducted on the devices being assessed, scientific literature from similar devices whose equivalence with the assessed device can be demonstrated or both clinical studies and scientific literature.

With respect to implantable devices or devices classified as Class III in the European Union, the manufacturer must conduct clinical studies to obtain the required clinical data, unless relying on existing clinical data from similar devices can be justified. As part of the conformity assessment process, depending on the type of devices, the Notified Body will review the manufacturer's clinical evaluation process, assess the clinical evaluation data of a representative sample of the device's subcategory or generic group, or assess all the clinical evaluation data, verify the manufacturer's assessment of that data and assess the validity of the clinical evaluation report and the conclusions drawn by the manufacturer.

Even after a manufacturer receives a CE Certificate of Conformity enabling the CE mark on it products and the right to sell the products in the EEA countries, a Notified Body or a competent authority may require post-marketing studies of the products. Failure to comply with such requirements in a timely manner could result in the withdrawal of the CE Certificate of Conformity and the recall or withdrawal of the subject product from the European market.

Table of Contents

A manufacturer must inform the Notified Body that carried out the conformity assessment of the medical devices of any planned substantial changes to the devices which could affect compliance with the Essential Requirements or the devices' intended purpose. The Notified Body will then assess the changes and verify whether they affect the product's conformity with the Essential Requirements or the conditions for the use of the devices. If the assessment is favorable, the Notified Body will issue a new CE Certificate of Conformity or an addendum to the existing CE Certificate of Conformity attesting compliance with the Essential Requirements. If it is not, the manufacturer may not be able to continue to market and sell the product in the EEA.

In the European Union, medical devices may be promoted only for the intended purpose for which the devices have been CE marked. Failure to comply with this requirement could lead to the imposition of penalties by the competent authorities of the European Union Member States. The penalties could include warnings, orders to discontinue the promotion of the medical device, seizure of the promotional materials and fines. Promotional materials must also comply with various laws and codes of conduct developed by medical device industry bodies in the European Union governing promotional claims, comparative advertising, advertising of medical devices reimbursed by the national health insurance systems and advertising to the general public.

Additionally, all manufacturers placing medical devices in the market in the European Union are legally bound to report any serious or potentially serious incidents involving devices they produce or sell to the competent authority in whose jurisdiction the incident occurred. In the European Union, manufacturers must comply with the EU Medical Device Vigilance System. Under this system, incidents must be reported to the relevant authorities of the European Union countries, and manufacturers are required to take Field Safety Corrective Actions, or FSCAs, to reduce a risk of death or serious deterioration in the state of health associated with the use of a medical device that is already placed on the market. An incident is defined as any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labeling or the instructions for use which, directly or indirectly, might lead to or might have led to the death of a patient or user or of other persons or to a serious deterioration in their state of health. An FSCA may include the recall, modification, exchange, destruction or retrofitting of the device. FSCAs must be communicated by the manufacturer or its European Authorized Representative to its customers and to the end users of the device through Field Safety Notices. In September 2012, the European Commission adopted a proposal for a regulation which, if adopted, will change the way that most medical devices are regulated in the European Union, and may subject products to additional requirements.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Sales of products will depend, in part, on the extent to which products are covered by third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations and the amount that will be paid. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors may

limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication. Additionally, the containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on investment in product development.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed to. Some

Table of Contents

countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements.

Healthcare Law and Regulation

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with third-party payors and customers are subject to broadly applicable fraud and abuse and other healthcare laws and regulations. Such restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- the federal False Claims Act imposes civil penalties, and provides for civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal transparency requirements under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the PPACA will require applicable manufacturers of covered drugs, devices, drugs and medical supplies to report to the Department of Health and Human Services information related to payments and other transfers of value to physicians and teaching hospitals and physician ownership and investment interests; and

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

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

Table of Contents

Sales and Marketing

We do not have a sales, marketing or distribution infrastructure and have limited experience in the sale, marketing and distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. We expect to build a commercial infrastructure to allow us to market and sell certain of our product candidates when approved, if any, using a specialty sales force in the United States, and we may choose to establish commercialization capabilities in select countries outside the United States.

Employees

As of November 21, 2016, we had 21 full-time employees, of which 16 employees were engaged in research and development and 5 employees provided general and administrative support. Of our employees, 10 have earned advanced degrees. Our employees are not represented by a labor union or covered by a collective bargaining agreement.

Table of Contents

MANAGEMENT

The following table sets forth information about our current executive officers and directors as of November 22, 2016.

Name	Age	Position
Jonathan M. Peacock	58	Chairman of the Board
Fabian Tenenbaum	43	Chief Executive Officer
Peter Fernandes	62	Chief Regulatory and Safety Officer
Deborah A. Quinn, M.D.	62	Chief Medical Officer
Martin Dekker	44	Vice President of Device Engineering and Supply
Amy Edmonds	44	Vice President of Clinical Operations and Administration
Parag Shah, Ph.D.	40	Vice President of Project Management and Distribution
Naseem Amin, M.D.[(1)(3)]	55	Director
Scott P. Bruder, M.D., Ph.D.[(2)]	54	Director
Mary Ann Cloyd[(1)(3)]	62	Director
Matthew Holt[(2)(3)]	39	Director
Jens Luehring[(1)]	43	Director
Andre V. Moura[(2)]	35	Director
Daniel Tassé	56	Director
Adam B. Weinstein	37	Director

(1) Member of the Audit Committee

(2) Member of the Compensation Committee

(3) Member of the Nominating and Corporate Governance Committee

Jonathan M. Peacock has served as the Chairman of our board of directors since June 2014 and previously served as our Chief Executive Officer and President from June 2014 to November 2016. Prior to joining us, Mr. Peacock served as the Chief Financial Officer of Amgen Inc., a biotechnology company, from September 2010 to January 2014. From November 2005 to September 2010, he served as Chief Financial and Administrative Officer of Novartis Pharmaceuticals AG, the Pharmaceuticals and Biotechnology division of Novartis AG. Mr. Peacock was a partner at McKinsey and Company, a global strategy consulting firm, from 1998 to 2005. Before that, he was a partner at Price Waterhouse LLP, a global accounting firm (now PricewaterhouseCoopers LLP), from 1993 to 1998. He currently serves on the board of directors of Kite

51

Table of Contents

Pharma, Inc., a biopharmaceutical company. Mr. Peacock has served in an executive capacity as Chairman of Arix Bioscience PLC since February 2016. Mr. Peacock received an M.A. degree in economics from the University of St. Andrews. We believe that Mr. Peacock is qualified to serve on our board of directors because of his global management experience, his experience as an officer of a public company in our industry, his financial expertise and his position as our Chief Executive Officer and President.

Fabian Tenenbaum has served as our Chief Executive Officer since November 2016. Mr. Tenenbaum previously served as our Chief Financial Officer and Chief Business Officer from February 2016 to November 2016. Mr. Tenenbaum joined us from Anterios, Inc. a clinical-stage biopharmaceutical company focused on the development of dermatology products, where he served as Chief Financial Officer and Chief Business Officer from 2014 to 2016. Prior to that, Mr. Tenenbaum served as Chief Executive Officer with Syneron Beauty from 2011 to 2014, and Chief Financial Officer and Executive Vice President of Syneron Medical from 2007 to 2011. Prior to Syneron Medical, Mr. Tenenbaum was Vice President Americas for Radiancy, Inc., from 2002 to 2006, and Director, Commercial Operations and Corporate Development at Sunlight Medical, Inc. from 1999 to 2002. Mr. Tenenbaum holds a Bachelor in Medicine (B.Md.) from Ben Gurion University, Israel and an MBA from Columbia Business School.

On September 20, 2016, we announced the planned transition of Mr. Tenenbaum, current Chief Financial Officer and Chief Business Officer, to Chief Executive Officer of the Company, succeeding Mr. Peacock, who will retain his position as Chairman of the Board. The Company expects the transition to be completed by year-end.

Peter Fernandes has been our Chief Regulatory Officer since May 2015. In this role he manages safety for us and is the Executive Lead for the INOpulse drug-device combination development program. Prior to joining us, Mr. Fernandes was Vice President of Global Regulatory Affairs at Ikaria Inc., from October 2012 to May 2015, and in this capacity also led our regulatory group since its inception in February of 2014. Previously, he led Regulatory Affairs and Quality Assurance for OptiNose, Inc. from October 2010 to September 2012, was Vice President US Drug Regulatory Affairs Respiratory and US DRA Respiratory Franchise Head for Novartis Pharmaceuticals from November 2007 to October 2010. He has also served as the Head of US Development Site and Vice President of Regulatory Affairs and Quality Assurance at Altana Pharma, a subsidiary of Nycomed Inc., and led the US Respiratory and GI Drug Regulatory Affairs group at Boehringer Ingelheim. Mr. Fernandes has an M. Pharm. from the Grant Medical College and a B. Pharm. from the K.M. K College of Pharmacy, both at the University of Bombay in India.

Deborah A. Quinn, M.D. served as our Vice President and Medical Lead for the INOpulse programs from January 2015 and has been our Chief Medical Officer since September 2015. Prior to joining us, Dr. Quinn held several positions at Novartis Pharmaceuticals AG from December 2006 to January 2015, most recently as medical director for both pulmonary arterial hypertension and heart failure programs. Previously, Dr. Quinn worked at the Massachusetts General Hospital from 1998 to 2011 where she was an Instructor in Medicine from 1998 to 2006 and a Clinical Assistant Professor in Medicine at Harvard Medical School from 2006 to 2011. Her postdoctoral training in Medicine and Pulmonary and Critical Care Fellowship were at Massachusetts General Hospital. She received an M.D. from the

University of Massachusetts Medical School.

Martin Dekker has served as our Vice President of Device Engineering since January 2015. Prior to joining us, Mr. Dekker held several positions at Spacelabs Healthcare, a company that develops and manufactures medical devices, from November 1998 to January 2015, most recently as Director of Global Operations Engineering. During his time at Spacelabs Healthcare, Mr. Dekker led and co-designed new products, developed and launched transformative manufacturing technologies and championed cross-functional quality/engineering projects. He is a member of the Institute of Electrical and Electronic Engineers. Mr. Dekker received a B.S. in electronics from Noordelijke Hogeschool Leeuwarden, the Netherlands.

Amy Edmonds has served as our Vice President of Clinical Operations and Administration since September 2015 with responsibilities for Clinical Operations, Contracts & Outsourcing, Human Resources and Information

Table of Contents

Technology. Ms. Edmonds has over twenty years of global Clinical Operations and Training experience. Prior to joining us in 2014, Ms. Edmonds was responsible for Ikaria's Clinical Operations and Contracts & Outsourcing departments from October 2012 to February 2014 and held several positions of increasing responsibility at Celgene from November 2002 through October 2012. During her time at Celgene, Ms. Edmonds served as Global Clinical Operations Lead for the Americas for multiple therapeutic programs, the Head of North America Monitoring, and the Head of Clinical Operations Training. Ms. Edmonds has also worked in Clinical Operations and Training for Pfizer, Knoll Pharmaceuticals and ICON Clinical Research. Ms. Edmonds holds a Bachelor's degree from the University of Richmond.

Parag Shah, Ph.D. has served as our Vice President of Project Management and Distribution since April 2016 with responsibilities for Project Management, Supply Distribution, Pre-Clinical and Business Development activities. Prior to joining Bellerophon, Dr. Shah was Principal Scientist at Pfizer from 2004 through 2010 where he was responsible for leading multiple parenteral and liquid formulation development teams. In addition, Dr. Shah was a member of multiple Limited Duration Teams including serving as Pfizer's Team Lead for the Nanoparticle Network responsible for internal and external evaluation of nanoparticle technologies. Dr. Shah joined Ikaria as Parenteral Development Lead in 2010 and assumed additional responsibilities in 2012 as Director, Pharmaceutical Science, covering both Pharmaceutical Development and Clinical Supply Management. Dr. Shah received his Bachelor's degree from Carnegie Mellon and his Ph.D. in Chemical Engineering from The University of Texas at Austin.

Naseem Amin has served as a member of our board of directors since June 2015. Dr. Amin had served as the Chief Scientific Officer of Smith and Nephew Plc until 2014. Previously, Dr. Amin was Senior Vice President, Business Development at Biogen Idec from 2005 to 2009 and was with Genzyme Corporation from 1999 to 2005, most recently as Head, International Business Development and where he has also led the clinical development of five currently marketed therapeutic products. Dr. Amin began his career at Baxter Healthcare Corporation, where he served as Director, Medical Marketing and Portfolio Strategy, Renal Division. Dr. Amin is a Venture Partner at Advent Life Sciences, serves as an Advisory Board member for Imperial College, Department of Biomedical Engineering, and serves as Chairman of OPEN-London, a non-profit organization focused on encouraging and mentoring South Asians from Pakistan who are interested in starting entrepreneurial companies. Dr. Amin received his medical degree from the Royal Free School of Medicine, London, and an MBA from the Kellogg Graduate School of Management, Northwestern University. We believe that Dr. Amin is qualified to serve on our board of directors because of his broad industry experience in the Biotech and Medical Device industry.

Scott Bruder has served as a member of our board of directors since May 2015. Dr. Bruder is currently an adjunct Professor of Biomedical Engineering at the Case Western Reserve University School of Medicine, where he previously served as an adjunct faculty member in the Department of Orthopaedic Surgery for thirteen years. Dr. Bruder served as the Chief Medical and Scientific Officer of Stryker Corporation from 2013 until 2014, and was the Chief Science and Technology Officer for Becton, Dickinson and Company from 2007 until 2013. Previously, Dr. Bruder has also held a number of senior executive and scientific roles at Johnson & Johnson, Anika Therapeutics and Osiris Therapeutics. Dr. Bruder recently served on an FDA Advisory Committee for Cellular, Tissue and Gene Therapies, and he continues to serve on several Academic Advisory Boards for biomedical engineering at leading universities. Dr. Bruder is a magna cum laude graduate from Brown University with a Sc.B. in Biology, and a

graduate of Case Western Reserve University School of Medicine, where he simultaneously earned an M.D. and a Ph.D. in stem cell biology. He obtained additional clinical training at the Albert Einstein Medical Center and the University of Pennsylvania. We believe that Dr. Bruder is qualified to serve on our board of directors because of his experience in medical devices, biotechnology, life sciences, and biomedical engineering.

Mary Ann Cloyd has served as a member of our board of directors since February 2016. From 1990 to 2015, Ms. Cloyd was a partner at PricewaterhouseCoopers LLP ("PwC"), where she served multinational corporate clients in a variety of industries, including the biotechnology and pharmaceutical industries. She was the Leader of the PwC Center for Board Governance from 2012 to 2015. Ms. Cloyd has also served on both PwC's Global and U.S. Boards. On the U.S. Board, she chaired the Risk Management, Ethics & Compliance Committee and the Partner Admissions Committee, and on the Global Board, she served on the Risk and Operations Committee and the

Table of Contents

Clients Committee. Ms. Cloyd is on the Board of Trustees of the PwC Charitable Foundation, Inc., and she previously served as President of the Foundation. Ms. Cloyd is currently the Chair of the UCLA Iris Cantor Women's Center Advisory Board. Ms. Cloyd earned a bachelor of business administration from Baylor University, summa cum laude. We believe that Ms. Cloyd is qualified to serve on our board of directors because of her experience in finance, senior management and corporate governance.

Matthew Holt has served as a member of our board of directors since February 2014. Since 2001, Mr. Holt has been employed by New Mountain Capital, a private equity group, where he currently serves as a Managing Director. Prior to joining New Mountain Capital, Mr. Holt served in the mergers and acquisitions Group at Lehman Brothers, a financial services firm. Mr. Holt has served on the board of directors of Ikaria since March 2007. Mr. Holt received an A.B. in English and American literature and language from Harvard College. We believe that Mr. Holt is qualified to serve on our board of directors because of his financial expertise and his years of experience providing strategic advisory services across many industries.

Jens Luehring has served as a member of our board of directors since January 2015. Mr. Luehring has been the Head of Finance, Americas, of The Linde Group since April 2012. In this position, his responsibilities include accounting, tax, business planning, investments, treasury and insurance. Prior to his current role, Mr. Luehring was the Head of Mergers & Acquisitions of The Linde Group from April 2007 to March 2012. Mr. Luehring received a Master of Business Economics from Hanover University in 1998. Prior to joining The Linde Group in January 2006, Mr. Luehring worked in investment banking, covering corporate finance, private equity, equity capital markets and mergers and acquisitions. We believe that Mr. Luehring is qualified to serve on our board of directors because of his financial, business and strategic expertise.

Andre V. Moura has served as a member of our board of directors since February 2014. Mr. Moura joined New Mountain Capital in 2005, where he currently serves as Managing Director. Prior to joining New Mountain Capital, Mr. Moura was employed by McKinsey & Company, a global management consulting firm. Mr. Moura also serves on the board of directors of two privately held companies. Mr. Moura received an A.B. in computer science from Harvard College and an M.B.A. from Harvard Business School. We believe that Mr. Moura is qualified to serve on our board of directors because of his financial expertise and his years of experience providing strategic advisory services to diverse companies across multiple industries.

Daniel Tassé has served as a member of our board of directors since February 2014. Prior to the acquisition of Ikaria by Mallinckrodt in April 2015, Mr. Tassé was President and Chief Executive Officer and Chairman of the board of directors of Ikaria and served as our Interim Chief Executive Officer and President from February 2014 to June 2014. Previously, Mr. Tassé was the General Manager of the Pharmaceuticals and Technologies Business Unit of Baxter International, Inc., a global diversified healthcare company and Vice President and Regional Director for Australasia at GlaxoSmithKline. Mr. Tassé currently serves as a Director of Indivior PLC, a London Stock Exchange publicly traded company, and serves on its Audit and Compensation committees. Mr. Tassé is a member of the Healthcare Leadership Council. He also is a member of the Health Section Governing Board of the Biotechnology Industry

Organization, where he participates on the bioethics, regulatory environment and reimbursement committees. Additionally, Mr. Tassé is a member of the Board of Directors of the Pharmaceutical Research and Manufacturers Association of America, where he participates on the FDA and biomedical research committee. Mr. Tassé received a B.S. in biochemistry from the University of Montreal. We believe Mr. Tassé is qualified to serve on our board of directors because of his former service as our Chief Executive Officer and President, his extensive track record of business building in the healthcare industry, his strong background within critical care, his global management experience and his detailed knowledge of the pharmaceutical industry, our company, employees, client base and competitors.

Adam B. Weinstein has served as a member of our board of directors since February 2014. He is a Managing Director of New Mountain Capital, LLC, and he joined that organization in 2005. At New Mountain, Mr. Weinstein serves as a Chief Financial Officer and is an Executive Vice President and is on the Board of Directors of New Mountain Finance Corporation, a publicly traded business development company. Prior to joining New Mountain, Mr. Weinstein held roles in the mergers and acquisitions and private equity investor services areas

Table of Contents

of Deloitte & Touche, LLP, in that firm's merger and acquisition and private equity investor services areas. Mr. Weinstein is a New York State Certified Public Accountant and received his B.S., summa cum laude, in accounting from Binghamton University. We believe that Mr. Weinstein is qualified to serve on our board of directors because of his financial and accounting expertise and valuable corporate governance experience.

Director Independence

NASDAQ rules require that a majority of our board of directors be independent within one year of listing, which in our case was February 13, 2015. In addition, the NASDAQ rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and corporate governance committees be independent and that audit committee members also satisfy independence criteria set forth in Rule 10A-3 under the Exchange Act. Under NASDAQ rules, a director will only qualify as an "independent director" if, in the opinion of our board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors or any other board committee, accept, directly or indirectly, any consulting, advisory or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries. Our board of directors has determined that Messrs. Bruder, Holt, Luehring, Moura, and Weinstein, Dr. Amin and Ms. Cloyd and are "independent directors," as defined under Rule 5605(a)(2) of the NASDAQ rules. In making such determination, our board of directors considered the relationships that each such 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.

The phase-in periods with respect to director independence under the applicable NASDAQ rules allow us to have only one independent member on each of the audit committee, compensation committee and nominating and corporate governance committee upon the listing date of our common stock, a majority of independent members on each of these committees within 90 days of the listing date and fully independent committees within one year of the listing date.

Our board of directors has determined that Mr. Leuhring, Dr. Amin and Ms. Cloyd, who are members of our audit committee, Messrs. Bruder and Moura, who are members of our compensation committee, and Mr. Amin and Ms. Cloyd, who are members of our nominating and corporate governance committee, satisfy the independence standards for their respective committees established by the SEC and NASDAQ rules, as applicable, including, in the case of the audit committee member, the independence requirements of Rule 10A-3 under the Exchange Act and, in the case of the compensation committee members, the independence requirements under Rule 10C-1 under the Exchange Act. In making such determinations, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances that our board of directors deemed relevant in determining independence, including the beneficial ownership of our capital stock by each non-employee director.

55

Table of Contents

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

The following is a description of transactions since January 1, 2015 to which we have been a party, and in which any of our directors, executive officers and holders of more than 5% of our voting securities and affiliates of our directors, executive officers and holders of more than 5% of our voting securities, had or will have a direct or indirect material interest. We believe that all of the transactions described below were made on terms no less favorable to us than could have been obtained from unaffiliated third parties.

Corporate Conversion

On February 12, 2015, we completed transactions pursuant to which we converted from a Delaware limited liability company into a Delaware corporation and changed our name to Bellerophon Therapeutics, Inc. As required by the limited liability company agreement of Bellerophon Therapeutics LLC, the conversion was approved by the board of directors of Bellerophon Therapeutics LLC. In connection with the Corporate Conversion, holders of our outstanding voting units received one share of voting common stock for each voting unit held immediately prior to the Corporate Conversion, holders of our outstanding non-voting units received one share of non-voting common stock for each non-voting unit held immediately prior to the Corporate Conversion and options to purchase non-voting units became options to purchase one non-voting share of common stock for each unit underlying such options immediately prior to the Corporate Conversion, at the same aggregate exercise price in effect prior to the Corporate Conversion.

Following the Corporate Conversion and prior to our registration statement being declared effective, certain entities affiliated with certain of our principal stockholders were merged with and into us. We refer to these mergers as the Mergers. In connection with the conversion and the Mergers, these certain entities affiliated with certain of our principal stockholders received, in exchange for their equity interests in the entities being merged into us, the number of shares of our common stock that they would have held had they held our equity interests directly.

In connection with the Corporate Conversion, we entered into the following agreements:

Merger Agreement

We entered into a merger agreement with certain of our principal stockholders to effect the Mergers. Concurrently with the consummation of the conversion to a corporation, our limited liability company agreement, or the LLC agreement, was terminated (other than the provisions thereof relating to certain pre-closing tax matters and liabilities

for breaches of the LLC agreement).

In the merger agreement, the companies that merged into us represented and warrantied that they did not have any liabilities, operations or businesses other than activities related to holding our common stock and other than liabilities for (i) deferred income taxes that reflect only timing differences between the treatment of items for accounting and income tax purposes and (ii) income taxes with respect to pre-closing periods which are not yet due and payable and for which we are fully indemnified. The Mergers were structured so that we did not acquire any assets (other than certain income tax receivables and an amount of cash that has been estimated in good faith to be sufficient to pay all pre-closing income taxes of the entities to be merged into us) or become responsible for any liabilities other than (i) deferred income taxes that reflect only timing differences between the treatment of items for accounting and income tax purposes and (ii) income taxes with respect to pre-closing periods which are not yet due and payable and for which we are fully indemnified. Each of our principal stockholders party to the merger agreement will indemnify us with respect to any liabilities (including tax liabilities related to pre-closing periods, other than with respect to deferred income tax liabilities that reflect only timing differences between the treatment of items for accounting and income tax purposes) of the entity related to such principal stockholder that we acquire in the merger. Any assets (other than our equity interests, certain income tax receivables and an amount of cash that has been estimated in good faith to be sufficient to pay all liabilities, including pre-closing income taxes, of the entities to be merged into us) in the entities to be merged into us were distributed to the equity holders of those entities prior to the Mergers.

Table of Contents

Registration Rights Agreement

We have entered into a registration rights agreement with certain holders of our common stock, including our 5% stockholders and their affiliates and entities affiliated with our directors. The registration rights agreement provides these holders the right to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing.

Stockholders Agreements

New Mountain Stockholders Agreement

In February 2015, in connection with our IPO, we entered into a stockholders agreement with the New Mountain Entities, which provides that the New Mountain Entities are entitled to designate one director for nomination to our board of directors, to designate one director to the board of directors (or equivalent governing body) of each of our subsidiaries and to appoint the lead director of our board of directors, in each case, for so long as the New Mountain Entities or certain of their respective assignees beneficially own (i) 50% or more of the sum of (a) the number of shares of our common stock that they owned immediately prior to the closing of our IPO and (b) the number of shares of common stock, if any, acquired following the closing of our IPO (subject to in each case adjustment in the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification or other similar change in our capitalization) and (ii) 15% or more of our common stock outstanding (as set forth on the cover of our then most recently filed annual report on Form 10-K or quarterly report on Form 10-Q). Subject to the same ownership thresholds, the director nominated by the New Mountain Entities is entitled to serve on each committee of our board of directors and of the board of directors (or equivalent governing body) of each of our subsidiaries and the consent of the New Mountain Entities is required to establish any new committee of our board of directors or the board of directors (or equivalent governing body) of any of our subsidiaries, in each case except to the extent prohibited by applicable law or applicable listing exchange rules.

The New Mountain Entities may assign their rights to designate one director for nomination to our board of directors, to designate a director to the board of directors (or equivalent governing body) of each of our subsidiaries and to appoint the lead director of our board of directors to a person who acquires, in a transaction other than a registered public offering or a sale pursuant to Rule 144 under the Securities Act, at least 50% of the aggregate number of shares of our common stock owned, directly or indirectly, by the New Mountain Entities as of immediately prior to such transaction.

In addition, the stockholders agreement provides that, we are required to obtain the prior written approval of the New Mountain Entities to take certain actions, including, among other things, actions to:

- consolidate or merge into or with any other person, sell, lease or transfer all or a significant portion of our assets or capital stock to another person or enter into any other similar business combination transaction, or effect a liquidation;
- authorize, issue, sell, offer for sale or solicit offers to buy any shares of our common stock or any convertible securities or any other equity or debt securities or rights to acquire any of our or our subsidiaries' equity or debt securities, subject to certain exceptions, including among other things, the issuance under our stock incentive plan of grants that have been approved by our board of directors (or a board committee) and at least one director appointed by the New Mountain Entities;
- incur indebtedness or refinance any indebtedness, in each case in an amount in excess of a specified threshold;
- hire or replace our chief executive officer; or
- agree or otherwise commit to do any of the foregoing (unless the commitment is conditioned on obtaining the approval of the New Mountain Entities).

These approval rights of the New Mountain Entities will terminate when the New Mountain Entities or certain of their respective assignees beneficially own either (i) less than 50% of the sum of (a) the aggregate number

Table of Contents

of shares of our common stock that they collectively owned immediately prior to the closing of our IPO and (b) the number of shares of our common stock, if any, acquired following the closing of our IPO (subject to in each case adjustment in the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification or similar changes in our capitalization) or (ii) less than 15% of our common stock outstanding (as set forth on the cover of our then most recently filed annual report on Form 10-K or quarterly report on Form 10-Q). As of November 8, 2016, the New Mountain Entities held approximately 33.5% of our outstanding common stock.

Linde Stockholders Agreement

In February 2015, in connection with our IPO, we also entered into a stockholders agreement with Linde, which provides that Linde is entitled to designate one director for nomination to our board of directors and to designate one director to the board of directors (or equivalent governing body) of each of our subsidiaries, in each case, for so long as Linde or certain of its assignees beneficially own (i) 50% or more of the sum of (a) the number of shares of our common stock that they owned immediately prior to the closing of our IPO and (b) the number of shares of common stock, if any, acquired following the closing of our IPO (subject to in each case adjustment in the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification or other similar change in our capitalization) and (ii) 10% or more of our common stock outstanding (as set forth on the cover of our then most recently filed annual report on Form 10-K or quarterly report on Form 10-Q). Subject to the same ownership thresholds, the director designated by Linde is entitled to serve on each committee of our board of directors and of the board of directors (or equivalent governing body) of each of our subsidiaries and the consent of Linde is required to establish any new committee of our board of directors or the board of directors (or equivalent governing body) of any of our subsidiaries, in each case except to the extent prohibited by applicable law or applicable listing exchange rules.

Linde may assign its rights to designate one director for nomination to our board of directors and to designate a director for nomination to the board of directors (or equivalent governing body) of each of our subsidiaries to a person who acquires, in a transaction other than a registered public offering or a sale pursuant to Rule 144 under the Securities Act, at least 50% of the aggregate number of shares of our common stock owned, directly or indirectly, by Linde as of immediately prior to such transaction. As of November 8, 2016, Linde held approximately 11.2% of our outstanding common stock.

Management Rights Letters

We have entered into management rights letters with entities affiliated with certain of our principal stockholders, pursuant to which such entities are entitled to routinely consult with and advise management regarding our operations and have the right to inspect our books and records. We will also be required to deliver financial statements to such entities within 45 days after the end of each of the first three quarters of each fiscal year and 120 days after the end of

each fiscal year and any other periodic reports as soon as they become available. Our management rights letter with the New Mountain Entities also provides that at any time during which the New Mountain Entities do not have the direct contractual right to designate a representative to serve on our board of directors, the New Mountain Entities will have the right to designate one observer to our board of directors. Such observer shall be entitled to attend all meetings of our board of directors and to receive copies of all materials provided to the directors, subject to customary exceptions specified in the management rights letter. Each management rights letter will terminate on the date the entity party thereto (or principal stockholder with which such entity is affiliated) no longer holds any of our securities.

Indemnification Agreements

Our certificate of incorporation provides that we will indemnify our directors and officers to the fullest extent permitted by Delaware law. In addition, we have entered into indemnification agreements with each of our directors and officers.

Relationship with Ikaria

Prior to the Spin-Out on February 12, 2014, we were a wholly-owned subsidiary of Ikaria. See “Business-Relationship with Ikaria after the Spin-Out.” Following the Spin-Out, Ikaria ceased to hold any of our equity

Table of Contents

interests and we became a stand-alone company. On April 16, 2015, Mallinckrodt announced that it had completed its acquisition of Ikaria.

Separation and Distribution Agreement

In connection with the Spin-Out, we and Ikaria entered into a separation and distribution agreement which sets forth the key provisions relating to the separation of our business from Ikaria's other businesses. The separation and distribution agreement described the assets and liabilities that remained with or were transferred to us and those that remained with or were transferred to Ikaria and the terms of Ikaria's distribution of all of our then outstanding units to its stockholders. The separation and distribution agreement provides for a full and complete release and discharge of all liabilities between Ikaria and us, except as set forth in the agreement. We and Ikaria each agreed to indemnify, defend and hold harmless the other party and its subsidiaries, and each of their respective past and present directors, officers and employees, and each of their respective permitted successors and assigns, from any and all damages relating to, arising out of or resulting from, among other things, our business and certain additional specified liabilities or Ikaria's business and certain additional specified liabilities, as applicable. The separation and distribution agreement also provides that we and Ikaria will each use reasonable best efforts, including by cooperating with the other party, to, among other things, effect the transfer of any assets being transferred in connection with the Spin-Out that had not been transferred as of the date of the Spin-Out.

In connection with the Spin-Out, we and Ikaria have entered into other agreements that will govern various interim and ongoing relationships between us and Ikaria. These agreements, the material terms of which are summarized below, include:

- transition services agreements;
- an exclusive cross-license, technology transfer, and regulatory matters agreement;
- an employee matters agreement;
- agreements not to compete; and
- drug and device supply agreements.

Services Agreements

Transition Services Agreement. In February 2014, we entered into the TSA. Pursuant to the terms and conditions of the TSA, Ikaria agreed to use commercially reasonable efforts to provide certain services to us, including human resources support, real estate support, information technology support, accounting and tax support, treasury support, financial planning and analysis support, purchasing support, management/executive services, legal services, quality services, regulatory services, drug and device safety services, business development support, biometrics support and manufacturing support. Ikaria was obligated, subject to the terms of the TSA (including the early termination provisions thereof and our obligation to use commercially reasonable efforts to provide the services for ourselves as soon as practicable), to provide such services until February 2016. Ikaria also agreed, on the terms and subject to the conditions of the TSA, to use commercially reasonable efforts to allow our employees to remain in Ikaria's Hampton, New Jersey facility for the continued operation of our business during the term of the TSA. In July 2015, we entered into an amendment to the TSA advancing the termination date from February 9, 2016 to September 30, 2015. Amounts incurred in 2015 totaled $7.0 million.

We were obligated to pay Ikaria a service fee in the amount of $772,000 per month and to reimburse Ikaria for any out-of-pocket expenses incurred in connection with its provisions of services under the TSA, any taxes imposed on Ikaria in connection with the performance or delivery of services under the TSA and any costs and expenses incurred by Ikaria in connection with the performance of any services that require resources outside of the existing resources of Ikaria or that otherwise interfere with the ordinary operations of Ikaria's business. This monthly service fee was payable by us regardless of the frequency or quantity of services actually utilized by us under the TSA. We were also obligated to pay any fees, costs, expenses or other amounts incurred by Ikaria to obtain the right to allow our employees to remain in the Hampton, New Jersey facility during the term of the TSA.

Table of Contents

At the time of the Spin-Out, we deposited the sum of $18.5 million into escrow, representing the aggregate of the $772,000 monthly service fees payable by us under the TSA, to guarantee payment of the monthly service fees by us. Pursuant to the July 2015 amendment, during October 2015, we received from escrow $3.3 million, which is equal to the amount it deposited to pay amounts owed to Ikaria under the TSA for the period from October 1, 2015 to February 9, 2016.

2015 Services Agreement. We entered into a services agreement with Ikaria, effective as of January 1, 2015, which we refer to as the 2015 Services Agreement. Pursuant to the terms of the 2015 Services Agreement, we had agreed to use commercially reasonable efforts to provide certain services to Ikaria, including services related to regulatory matters, drug and device safety, clinical operations, biometrics and scientific affairs. We were obligated, subject to the terms of the 2015 Services Agreement, to provide such services until February 2016. In July 2015, we entered into an amendment to the 2015 Services Agreement advancing the termination date from February 8, 2016 to September 30, 2015. In connection with the execution of the 2015 Services Agreement, Ikaria paid us a one-time service fee in the amount of $916,666 and was obligated to pay us a service fee in the amount of $83,333 per month, subject to our obligation to perform the services.

In addition, pursuant to the terms and conditions of the 2015 Services Agreement, Ikaria had agreed to use commercially reasonable efforts to provide certain services to us, including services related to information technology, and servicing and upgrades of INOpulse devices. Ikaria was obligated, subject to the terms of the 2015 Services Agreement, to provide such services until February 2016. We were obligated to pay Ikaria certain fees under the 2015 Services Agreement that total, in the aggregate, approximately $215,000, subject to termination of the 2015 Services Agreement. In July 2015, we entered into an amendment to the 2015 Services Agreement advancing the termination date from February 8, 2016 to September 30, 2015. Amounts incurred in 2015 total $0.2 million.

Exclusive Cross-License, Technology Transfer and Regulatory Matters Agreement

In February 2014, we entered into an exclusive cross-license, technology transfer and regulatory matters agreement with Ikaria. Pursuant to the terms of the license agreement, Ikaria granted to us a fully paid-up, non-royalty bearing, exclusive license under specified intellectual property rights controlled by Ikaria to engage in the development, manufacture and commercialization of nitric oxide, devices to deliver nitric oxide and related services for or in connection with out-patient, chronic treatment of patients with PAH, PH-COPD or PH-IPF, which we refer to collectively as the Bellerophon indications. In November 2015, we entered into an amendment to our exclusive cross-license, technology transfer and regulatory matters agreement with Ikaria that included a royalty equal to 3% of net sales of any commercial products for PAH.

On July 27, 2015, we entered into an amendment to the license agreement to expand the scope of our license to allow the Company to develop our INOpulse program for the treatment of three additional indications: chronic

thromboembolic pulmonary hypertension, or CTEPH, pulmonary hypertension associated with sarcoidosis and pulmonary hypertension associated with pulmonary edema from high altitude sickness. Subject to the terms set forth therein, the amendment to the license agreement also provides that we will pay Ikaria a royalty equal to 5% of net sales of any commercialized products for the three additional indications.

We have granted to Ikaria a fully paid-up, non-royalty-bearing, exclusive license under specified intellectual property rights that we control to engage in the development, manufacture and commercialization of products and services for or used in connection with the diagnosis, prevention or treatment, whether in- or out-patient, of certain conditions and diseases other than the Bellerophon indications and for the use of nitric oxide to treat or prevent conditions that are primarily managed in the hospital, which we refer to collectively as the Ikaria nitric oxide business.

We have agreed that, during the term of the license agreement, we will not, without the prior written consent of Ikaria, grant a sublicense under any of the intellectual property licensed to us under the license agreement to any of our affiliates or any third party, in either case, that directly or indirectly competes with the Ikaria nitric oxide business. We have also agreed that we will include certain restrictions in our agreements with customers of our products to ensure that such products will only be used for the Bellerophon indications.

Table of Contents

The license agreement will expire on a product-by-product basis for products for a specific Bellerophon indication at such time as we are no longer developing or commercializing any product for such indication. The license agreement may be terminated by either party in the event an act or order of a court or governmental authority prohibits either party from substantially performing under the license agreement. Either party may also terminate the license agreement in the event of an uncured material breach by the other party or in the event the other party is insolvent or in bankruptcy proceedings. Ikaria may also terminate the license agreement if we or any of our affiliates breach the agreements not to compete described below, or if we or any successor to our rights under the license agreement markets a generic nitric oxide product that is competitive with INOmax. Under certain circumstances, if the license agreement is terminated, the licenses granted to Ikaria by us will survive such termination.

Employee Matters Agreement

In February 2014, we entered into an employee matters agreement with Ikaria, pursuant to which the employment of certain Ikaria employees was transferred to us or our subsidiaries on the terms and conditions set forth therein. The employee matters agreement also sets forth the treatment of outstanding Ikaria stock options and RSUs in connection with the Spin-Out. We have agreed to assume and pay, perform, fulfill and discharge, in accordance with the terms of the employee matters agreement, all liabilities to or relating to such transferred employees. Effective as of the date of the Spin-Out, such transferred employees terminated participation in Ikaria's employee benefit plans, and we or our subsidiaries adopted employee benefit plans substantially similar to the following Ikaria plans: a 401(k) plan, a medical and dental plan, long-term disability, short-term disability, life and accidental death and dismemberment and flexible spending accounts, pursuant to the terms of the employee matters agreement.

Agreements Not to Compete

In September 2013, October 2013 and February 2014, we and each of our subsidiaries entered into an agreement not to compete with a subsidiary of Ikaria, each of which was amended in July 2015, or, collectively, the agreements not to compete. Pursuant to the agreements not to compete, as amended, we and each of our subsidiaries agreed not to engage, anywhere in the world, in any manner, directly or indirectly, until the earlier of five years after the effective date of such agreement not to compete amendments or the date on which Ikaria and all of its subsidiaries are no longer engaged in such business, in:

- the development, manufacture, commercialization, promotion, sale, import, export, servicing, repair, training, storage, distribution, transportation, licensing or other handling or disposition of any product or service (including, without limitation, any product or service that utilizes, contains or includes nitric oxide for inhalation, a device intended to deliver nitric oxide or a service that delivers or supports the delivery of nitric oxide), bundled or unbundled, for or used in connection with (a) the diagnosis, prevention or treatment, in both adult and/or pediatric populations, and whether in- or out-patient, of: (i) hypoxic respiratory failure associated with pulmonary

hypertension, (ii) pulmonary hypertensive episodes and right heart failure associated with cardiovascular surgery, (iii) bronchopulmonary dysplasia, (iv) the management of ventilation-perfusion mismatch in acute lung injury, (v) the management of ventilation-perfusion mismatch in acute respiratory distress syndrome, (vi) the management of pulmonary hypertension episodes and right heart failure in congestive heart failure, (vii) pulmonary edema from high altitude sickness, (viii) the management of pulmonary hypertension episodes and right heart failure in pulmonary or cardiac surgery, (ix) the management of pulmonary hypertension episodes and right heart failure in organ transplant, (x) sickle cell vaso-occlusive crisis, (xi) hypoxia associated with pneumonia or (xii) ischemia-reperfusion injury or (b) the use of nitric oxide to treat or prevent conditions that are primarily managed in the hospital; or

- any and all development, manufacture, commercialization, promotion, sale, import, export, storage, distribution, transportation, licensing, or other handling or disposition of any terlipressin or any other product within the pressin family, (a) intended to treat (i) hepatorenal syndrome in any form, (ii) bleeding esophageal varices or (iii) septic shock or (b) for or in connection with the management of low blood pressure.

The agreements not to compete expressly exclude the Bellerophon indications.

61

Table of Contents

Supply Agreements

Device Clinical Supply Agreement. In February 2014, we entered into the device supply agreement, pursuant to which Ikaria will use commercially reasonable efforts to manufacture and supply our requirements for certain nitric oxide delivery devices specified in the device supply agreement for use in our clinical programs for PAH and PH-COPD. Pursuant to the device supply agreement, we will pay to Ikaria an amount equal to Ikaria's internal and external manufacturing cost plus 20%. The device supply agreement expired on February 9, 2015.

Drug Clinical Supply Agreement. In February 2014, we entered into the drug supply agreement, pursuant to which Ikaria has agreed to use commercially reasonable efforts to manufacture and supply, and we have agreed to acquire from Ikaria, our requirements for nitric oxide for inhalation and corresponding placebo for use in our clinical programs for PAH, PH-COPD and PH-IPF. Under the terms of the drug supply agreement, we have also granted Ikaria a right of first negotiation in the event that we desire to obtain supply of nitric oxide for inhalation and corresponding placebo (or any variant thereof or any version with different specifications) for commercial use. The drug supply agreement will expire on a product-by-product basis on the date we discontinue clinical development of such product. In addition, either party may terminate the drug supply agreement in the event of an uncured material breach by the other party.

In November 2015, we amended our drug supply agreement with Ikaria to secure future supply and pricing for cartridges and nitric oxide. Under the amended supply agreement, we paid Ikaria $6.6 million, $0.6 million of which was applied to outstanding amounts owed to Ikaria under the drug supply agreement. The remaining $6.0 million resulted in a prepayment to Ikaria in exchange for defined levels of cartridges and nitric oxide. The amendment to the agreement also fixes pricing for any additional cartridges or nitric oxide beyond the defined levels. Additionally, the amendment requires us to pay to Ikaria an additional $1.75 million upon successful completion of the initial PAH phase 3 clinical trial and a perpetual royalty calculated as 3% of PAH sales on a quarterly basis.

Participation in Initial Public Offering

In our IPO, certain of our directors, executive officers and 5% stockholders and their affiliates purchased an aggregate of 1,914,464 shares of our common stock. Each of those purchases was made through the underwriters or through the directed share program at the IPO price of $12.00 per share. The following table sets forth the aggregate number of shares of our common stock that these directors, executive officers and 5% stockholders and their affiliates purchased in our IPO:

Purchaser[(1)]

	Shares of common stock	Total purchase price
New Mountain Entities	1,070,166	12,841,992
Linde	358,916	4,306,992
ARCH	212,666	2,551,992
Venrock	211,916	2,542,992
Jonathan M. Peacock	20,800	249,600
Manesh Naidu	1,500	18,000
Reinilde Heyrman	1,500	18,000
Martin Meglasson	12,000	144,000
Daniel Tassé	25,000	300,000

(1) See “Principal Stockholders” for more information about the shares held by the below identified entities, directors and executive officers.

Table of Contents

Entities affiliated with New Mountain Capital, LLC and Linde North America, existing stockholders, have agreed to purchase an aggregate of 7,634,286 Class A Units. The placement agent will receive a fee of 4.0% from any shares of our common stock purchased by these parties.

Policies and Procedures for Related Person Transactions

Our board of directors has adopted written policies and procedures for the review of any transaction, arrangement or relationship in which we were or are to be a participant, the amount involved exceeds $120,000 and one of our executive officers, directors, director nominees or 5% stockholders, or their immediate family members, each of whom we refer to as a "related person," has a direct or indirect material interest.

If a related person proposes to enter into such a transaction, arrangement or relationship, which we refer to as a "related person transaction," the related person must report the proposed related person transaction to our General Counsel or Chief Financial Officer, or in each case an individual performing similar functions. The policy calls for the proposed related person transaction to be reviewed and, if deemed appropriate, approved by our audit committee. Whenever practicable, the reporting, review and approval will occur prior to entry into the transaction. If advance review and approval is not practicable, the audit committee will review, and, in its discretion, may ratify the related person transaction. The policy also permits the chairman of the audit committee to review and, if deemed appropriate, approve proposed related person transactions that arise between committee meetings, subject to ratification by the committee at its next meeting. Any related person transactions that are ongoing in nature will be reviewed annually.

A related person transaction reviewed under the policy will be considered approved or ratified if it is authorized by the audit committee after full disclosure of the related person's interest in the transaction. As appropriate for the circumstances, the committee will review and consider:

- the related person's interest in the related person transaction;
- the approximate dollar value of the amount involved in the related person transaction;
- the approximate dollar value of the amount of the related person's interest in the transaction without regard to the amount of any profit or loss;
- whether the transaction was undertaken in the ordinary course of our business;

- whether the terms of the transaction are no less favorable to us than terms that could have been reached with an unrelated third party;

- the purpose of, and the potential benefits to us of, the transaction; and

- any other information regarding the related person transaction or the related person in the context of the proposed transaction that would be material to investors in light of the circumstances of the particular transaction.

The audit committee may approve or ratify the transaction only if the committee determines that, under all of the circumstances, the transaction is in our best interests. The committee may impose any conditions on the related person transaction that it deems appropriate.

In addition to the transactions that are excluded by the instructions to the SEC's related person transaction disclosure rule, our board of directors has determined that the following transactions do not create a material direct or indirect interest on behalf of related persons and, therefore, are not related person transactions for purposes of this policy:

Table of Contents

- interests arising solely from the related person's position as an executive officer of another entity (whether or not the person is also a director of such entity) that is a participant in the transaction, where (a) the related person and all other related persons own in the aggregate less than a 10% equity interest in such entity, (b) the related person and his or her immediate family members are not involved in the negotiation of the terms of the transaction and do not receive any special benefits as a result of the transaction and (c) the amount involved in the transaction is less than the greater of $200,000 or 5% of the annual gross revenues of the company receiving payment under the transaction; and

- a transaction that is specifically contemplated by provisions of our charter or bylaws.

The policy provides that transactions involving compensation of executive officers shall be reviewed and approved by the compensation committee in the manner specified in its charter.

We did not have a written policy regarding the review and approval of related person transactions prior to our IPO. Nevertheless, with respect to such transactions, it was our policy for our board of directors to consider the nature of and business reason for such transactions, how the terms of such transactions compared to those which might be obtained from unaffiliated third parties and whether such transactions were otherwise fair to and in the best interests of, or not contrary to, our best interests. In addition, all related person transactions required prior approval, or later ratification, by our board of directors.

Participation in this Offering

Entities affiliated with New Mountain Capital, LLC and Linde North America, existing stockholders, have agreed to purchase an aggregate of 7,634,286 Class A Units.

Table of Contents

PRINCIPAL STOCKHOLDERS

The following table sets forth information regarding beneficial ownership of our capital stock as of November 22, 2016, by:

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

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our common stock. Shares of our common stock subject to options that are currently exercisable or exercisable within 60 days of November 21, 2016 are considered outstanding and beneficially owned by the person holding the options for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person. Except as otherwise noted, to our knowledge, the persons and entities in this table have sole voting and investing power with respect to all of the shares of our common stock beneficially owned by them, subject to community property laws, where applicable. The information is not necessarily indicative of beneficial ownership for any other purpose.

Entities affiliated with New Mountain Capital, LLC and Linde North America, existing stockholders, have indicated an interest in purchasing units in this offering at the offering price. The following table does not reflect any potential purchases by these existing stockholders or their affiliated entities.

The percentage ownership calculations for beneficial ownership are based on 14,559,766 shares of common stock outstanding as of November 22, 2016. The percentage of common stock beneficially owned after the offering reflects the sale of all 17,142,858 Class A Units at the public offering price. The percentage ownership information after this offering assumes no exercise of the warrants to be issued in this offering.

Except as otherwise set forth below, the address of the beneficial owner is c/o Bellerophon Therapeutics, Inc., 184 Liberty Corner Road, Suite 302, Warren, NJ 07059.

Name of Beneficial Owner	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned		Percentage of Shares Beneficially Owned Following the Offering	
5% Stockholders					
New Mountain Entities(1)	4,859,885	33.4	%	33.4	%
Linde(2)	1,629,804	11.2	%	11.2	%
Fidelity Investments (FMR LLC)(3)	1,302,070	8.9	%	4.1	%
ARCH(4)	965,660	6.6	%	3.0	%
Venrock(5)	962,415	6.6	%	3.0	%
Executive Officers and Directors					
Jonathan M. Peacock	222,702	1.5	%	*	
Fabian Tenenbaum	-	*		*	
Peter Fernandes	35,722	*		*	
Deborah Quinn	31,244	*		*	
Amy Edmonds	23,213	*		*	
Martin Dekker	23,181	*		*	
Parag Shah	8,881	*		*	
Naseem Amin	23,365	*		*	
Scott Bruder	18,692	*		*	
Matthew S. Holt(6)	4,859,885	33.4	%	33.4	%
Jens Luehring(7)	1,629,804	11.2	%	11.2	%
Andre V. Moura	20,716	*		*	
Daniel Tassé	145,254	1.0	%	*	
Adam B. Weinstein(8)	4,859,885	33.4	%	33.4	%
All executive officers and directors as a group (14 persons)	7,199,376	49.4	%	46.8	%

Table of Contents

*Less than one percent.

(1) Based on information provided in a Schedule 13G filed by New Mountain Investments II, LLC on February 16, 2016, consists of 346,974 shares held by Allegheny New Mountain Partners, L.P., 80,165 shares held by New Mountain Affiliated Investors II, L.P., 3,842,663 shares held by New Mountain Partners II (AIV-A), L.P. and 590,083 shares held by New Mountain Partners II (AIV-B), L.P. The general partner of each of the New Mountain Entities is New Mountain Investments II, L.L.C. and the manager of each of the New Mountain Entities is New Mountain Capital L.L.C. Steven Klinsky is the managing member of New Mountain Investments II, L.L.C. Adam Weinstein, a member of our board of directors, is a member of New Mountain Investments II, L.L.C. Matthew Holt, a member of our board of directors, is a member of New Mountain Investments II, L.L.C. New Mountain Investments II, L.L.C. has decision-making power over the disposition and voting of shares of portfolio investments of each of the New Mountain Entities. New Mountain Capital, L.L.C. also has voting power over the shares of portfolio investments of the New Mountain Entities in its role as the investment advisor. New Mountain Capital, L.L.C. is a wholly-owned subsidiary of New Mountain Capital Group, L.L.C. New Mountain Capital Group, L.L.C. is 100% owned by Steven Klinsky. Since New Mountain Investments II, L.L.C. has decision-making power over the New Mountain Entities, Mr. Klinsky may be deemed to beneficially own the shares that the New Mountain Entities hold of record or may be deemed to beneficially own. Mr. Klinsky, Mr. Weinstein, Mr. Holt, New Mountain Investments II, L.L.C. and New Mountain Capital, L.L.C. disclaim beneficial ownership over the shares held by the New Mountain Entities, except to the extent of their pecuniary interest therein. The address of the New Mountain Entities is c/o New Mountain Capital, L.L.C., 787 Seventh Avenue, 48th Floor, New York, New York 10019.

(2) Consists of 1,629,804 shares held by Linde North America, Inc., an indirect wholly-owned subsidiary of Linde AG. Jens Luehring, a member of our board of directors, is a director and chief financial officer of Linde North America, Inc. Mr. Luehring disclaims beneficial ownership of all shares held by Linde, except to the extent of his pecuniary interest therein, if any. The address of Linde North America, Inc. is 575 Mountain Avenue, Murray Hill, New Jersey 07974.

(3) Based on information provided in a Schedule 13G/A filed by FMR LLC on February 12, 2016. Edward C. Johnson 3d, a Director and Chairman of FMR LLC, and Abigail P. Johnson, a Director, Vice Chairman, and the Chief Executive Officer of FMR LLC, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B stockholders have entered into a stockholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the stockholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, as amended, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Edward C. Johnson 3d nor Abigail P. Johnson has the sole power to vote or direct the voting of the shares owned directly by the various investment companies registered under the Investment Company Act, which we refer to as the Fidelity Funds, advised by Fidelity Management & Research Company, which we refer to as FMR Co, a wholly owned subsidiary of FMR LLC, which power

Table of Contents

resides with the Fidelity Funds' Boards of Trustees. FMR Co carries out the voting of the shares under written guidelines established by the Fidelity Funds' Boards of Trustees. FMR LLC reports that it holds sole dispositive power with respect to 1,292,882 shares. The address of FMR LLC is 245 Summer Street, Boston, Massachusetts 02210.

(4) Based on information provided in a Schedule 13D filed by Arch Venture Fund VI LP on February 25, 2016 consists of 965,660 shares held by ARCH Venture Fund VI, L.P., or ARCH VI. ARCH Venture Partners VI, L.P., or the GPLP, as the sole general partner of ARCH VI, may be deemed to beneficially own certain of the shares held of record by ARCH VI. The GPLP disclaims beneficial ownership of all shares held of record by ARCH VI in which the GPLP does not have an actual pecuniary interest. ARCH Venture Partners VI, LLC, or the GPLLC, as the sole general partner of the GPLP, may be deemed to beneficially own certain of the shares held of record by ARCH VI. The GPLLC disclaims beneficial ownership of all shares held of record by ARCH VI in which it does not have an actual pecuniary interest. Keith Crandell, Clinton Bybee and Robert Nelsen are the managing directors of the GPLLC and may be deemed to beneficially own certain of the shares held of record by ARCH VI. The managing directors disclaim beneficial ownership of all shares held of record by ARCH VI in which they do not have an actual pecuniary interest. ARCH VI reports that it holds shared voting power and shares dispositive power with respect to 965,660 shares. The address of ARCH VI is 8725 West Higgins Road, Suite 290, Chicago, Illinois 60631.

(5) Based on information provided in a Schedule 13D filed by Venrock Associates IV LP on February 25, 2016 consists of 783,407 shares held by Venrock Associates IV, L.P.; 159,761 shares that are held by Venrock Partners, L.P. and 19,247 shares that are held by Venrock Entrepreneurs Fund IV, L.P. Venrock Management IV, LLC, Venrock Partners Management, LLC and VEF Management IV, LLC are the sole general partners of Venrock Associates IV, L.P., Venrock Partners, L.P. and Venrock Entrepreneurs Fund IV, L.P., respectively. Venrock Management IV, LLC, Venrock Partners Management, LLC and VEF Management IV, LLC disclaim beneficial ownership of all shares held by Venrock Associates IV, L.P., Venrock Partners, L.P. and Venrock Entrepreneurs Fund IV, L.P., except to the extent of their pecuniary interest therein. The address of Venrock is 3340 Hillview Avenue, Palo Alto, California 94304.

(6) Includes 346,974 shares held by Allegheny New Mountain Partners, L.P., 80,165 shares held by New Mountain Affiliated Investors II, L.P., 3,842,663 shares held by New Mountain Partners II (AIV-A), L.P. and 590,083 shares held by New Mountain Partners II (AIV-B), L.P. The general partner of each of the New Mountain Entities is New Mountain Investments II, L.L.C. and the manager of each of the New Mountain Entities is New Mountain Capital L.L.C. Matthew Holt, a member of our board of directors, is a member of New Mountain Investments II, L.L.C. New Mountain Investments II, L.L.C. has decision-making power over the disposition and voting of shares of portfolio investments of each of the New Mountain Entities. New Mountain Capital, L.L.C. also has voting power over the shares of portfolio investments of the New Mountain Entities in its role as the investment advisor. New Mountain Capital, L.L.C. is a wholly-owned subsidiary of New Mountain Capital Group, L.L.C. Mr. Holt disclaims beneficial ownership over the shares held by the New Mountain Entities, except to the extent of his pecuniary interest therein.

(7) Consists of 1,629,804 shares held by Linde North America, Inc., an indirect wholly-owned subsidiary of Linde AG. Jens Luehring, a member of our board of directors, is a director and the chief financial officer of Linde North

America, Inc. Mr. Luehring disclaims beneficial ownership of all shares held by Linde, except to the extent of his pecuniary interest therein, if any.

(8) Consists of 346,974 shares held by Allegheny New Mountain Partners, L.P., 80,165 shares held by New Mountain Affiliated Investors II, L.P., 3,842,663 shares held by New Mountain Partners II (AIV-A), L.P. and 590,083 shares held by New Mountain Partners II (AIV-B), L.P. The general partner of each of the New Mountain Entities is New Mountain Investments II, L.L.C. and the manager of each of the New Mountain Entities is New Mountain Capital L.L.C. Adam Weinstein, a member of our board of directors, is a member of New Mountain Investments II, L.L.C. New Mountain Investments II, L.L.C. has decision-making power over the disposition and voting of shares of portfolio investments of each of the New Mountain Entities. New Mountain Capital, L.L.C. also has voting power over the shares of portfolio

Table of Contents

investments of the New Mountain Entities in its role as the investment advisor. New Mountain Capital, L.L.C. is a wholly-owned subsidiary of New Mountain Capital Group, L.L.C. Mr. Weinstein disclaims beneficial ownership over the shares held by the New Mountain Entities, except to the extent of his pecuniary interest therein.

(9) Includes all options and/or warrants that are exercisable on or within 60 days from November 22, 2016 by the beneficial owner, except as otherwise noted.

Table of Contents

DESCRIPTION OF CAPITAL STOCK

General

The following description of our capital stock and provisions of our certificate of incorporation and bylaws are summaries and are qualified by reference to the certificate of incorporation and the bylaws that will be in effect upon the closing of this offering. We have filed copies of these documents with the SEC as exhibits to our registration statement of which this prospectus forms a part. The description of the capital stock reflects changes to our capital structure that will occur upon the closing of this offering.

As of November 22, 2016, our authorized capital stock consists of 125,000,000 shares of our common stock, $0.01 par value per share, and 5,000,000 shares of our preferred stock, $0.01 par value per share, all of which preferred stock will be undesignated.

As of November 22, 2016, we had issued and outstanding:

- 14,559,766 shares of our common stock held by 237 stockholders of record; and
- 1,444,416 shares of common stock issuable upon the exercise of outstanding stock options, at a weighted average exercise price of $6.76 per share.

Common Stock

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. Each election of directors by our stockholders will be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of outstanding preferred stock.

In the event of our liquidation or dissolution, the holders of our common stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the

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

Preferred Stock

Pursuant to our certificate of incorporation, we are authorized to issue “blank check” preferred stock, which may be issued from time to time in one or more series upon authorization by our Board of Directors. Our Board of Directors, without further approval of the stockholders, is authorized to fix the designations, powers, including voting powers, preferences and the relative, participating, optional or other special rights of the shares of each series and any qualifications, limitations and restrictions thereof. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes could, among other things, adversely affect the voting power or other rights of the holders of our common stock and, under certain circumstances, make it more difficult for a third party to gain control of us, discourage bids for our common stock at a premium or otherwise adversely affect the market price of the common stock.

Table of Contents

Options

As of November 22, 2016 we had outstanding options to purchase 1,444,416 shares of our common stock, at a weighted average exercise price of $6.76 per share.

Stockholders Agreements

See “Certain Relationships and Related Party Transactions” for a description of our stockholders agreements.

Management Rights Letters

See “Certain Relationships and Related Party Transactions” for a description of our management rights letters.

Registration Rights Agreement

See “Certain Relationships and Related Party Transactions” for a description of our registration rights agreements.

Delaware Anti-Takeover Law and Certain Charter and Bylaw Provisions

Delaware Law

From and after the first time that neither the New Mountain Entities and their affiliates, nor any of their qualified transferees, beneficially owns 15% or more of our outstanding common stock (as set forth as outstanding on the cover of our then most recently filed annual report on Form 10-K or quarterly report on Form 10-Q), we will be subject to Section 203 of the Delaware General Corporation Law. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a “business combination” with any “interested stockholder” for three years following the date that the person became an interested stockholder, unless either the interested stockholder attained

such status with the approval of our board of directors, the business combination is approved by our board of directors and stockholders in a prescribed manner or the interested stockholder acquired at least 85% of our outstanding voting stock in the transaction in which it became an interested stockholder. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person. The restrictions contained in Section 203 are not applicable to any of our existing stockholders that will own 15% or more of our outstanding voting stock upon the closing of this offering.

Staggered Board; Removal of Directors

Our certificate of incorporation and our bylaws divide our board of directors into three classes with staggered three-year terms. In addition, a director may be removed only for cause and only by the affirmative vote of the holders of at least 75% of the outstanding shares of our common stock. In addition, the authorized number of our directors may be changed only by resolution of our directors, and any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

The classification of our board of directors and the limitations on the ability of our stockholders to change the authorized number of directors, remove directors and fill vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our company.

Stockholder Action; Special Meeting of Stockholders; Advance Notice Requirements for Stockholder Proposals and Director Nominations

Our certificate of incorporation and our bylaws provide that any action required or permitted to be taken by our stockholders at an annual meeting or special meeting of stockholders may only be taken if it is properly brought

Table of Contents

before such meeting and may not be taken by written action in lieu of a meeting. Our certificate of incorporation and our bylaws also provide that, except as otherwise required by law, special meetings of the stockholders can only be called by the chairman of our board of directors, our chief executive officer or our board of directors. In addition, our bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of candidates for election to our board of directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors, or by a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of our outstanding voting securities. These provisions also could discourage a third party from making a tender offer for our common stock, because even if it acquired a majority of our outstanding voting stock, it would be able to take action as a stockholder, such as electing new directors or approving a merger, only at a duly called stockholder meeting and not by written consent.

Super-Majority Voting

The Delaware General Corporation Law provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless a corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Our bylaws may be amended or repealed by a majority vote of our board of directors or the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any election of directors is required to amend, repeal or adopt any provisions inconsistent with any of the provisions of our certificate of incorporation described above.

Exclusive Forum

Our certificate of incorporation provides that the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for (i) any derivative action or proceeding brought on behalf of our company, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors or officers to the company or our stockholders, (iii) any action asserting a claim against our company arising pursuant to any provision of the Delaware General Corporation Law or our certificate of incorporation or bylaws or (iv) any action asserting a claim against our company or any of our directors or officers governed by the internal affairs doctrine. Although our certificate of incorporation contains the provision described above, it is possible that a court could rule that such a provision is inapplicable for a particular claim or action or that such provision is unenforceable.

Demand Registration Rights

At any time or from time to time, subject to specified limitations set forth in the registration rights agreement and to any lock-up period, the New Mountain Entities or the holders of 10% of our then outstanding shares of common stock, may at any time demand in writing that we register all or a portion of the shares having rights under the registration rights agreement, which we refer to as the registrable shares, under the Securities Act if the total amount of registrable shares registered have an aggregate offering price of at least $10.0 million, unless the registration is of the balance of the registrable shares held by all the parties to the registration rights agreement. We are not obligated to effect a registration pursuant to this provision on more than six occasions in the case of demands made by the New Mountain Entities, or on more than two occasions in the aggregate in the case of demands made by the other parties to the agreement, and we are not obligated to effect a registration pursuant to this provision within 90 days of the effective date of any other registration statement that we may file pursuant to a demand registration.

Form S-3 Registration Rights

In addition, at any time after we become eligible to file a registration statement on Form S-3, subject to specified limitations set forth in the registration rights agreement, either the New Mountain Entities or the holders in the aggregate of 10% or more of our outstanding shares of common stock may demand in writing that we register on

Table of Contents

Form S-3 all or a portion of the registrable shares so long as the total amount of registrable shares being registered have an aggregate offering price of at least $10.0 million, unless the registration is of the balance of the registrable shares held by all the parties to the registration rights agreement.

Incidental Registration Rights

If, at any time after the closing of this offering, we propose to file a registration statement under the Securities Act, subject to certain exceptions set forth in the registration rights agreement, the holders of registrable shares will be entitled to notice of the registration and, subject to specified exceptions in the case of an underwritten offering, including market conditions, have the right to require us to register all or a portion of the registrable shares then held by them. The holders of registration rights under the registration rights agreement have waived these rights as they may apply to the filing of the registration statement of which this prospectus is a part.

Underwritten Public Offering

In the event that any registration in which the holders of registrable shares participate pursuant to the registration rights agreement is an underwritten public offering, we agree to enter into an underwriting agreement containing customary representation and warranties and covenants, including without limitation customary provisions with respect to indemnification of the underwriters of such offering. Holders of registrable securities must agree to any such underwriting agreement as a condition to participation in the offering. If the total number of shares, including registrable shares, requested by holders to be included in such offering exceeds the largest number of shares to be sold (other than by us) that the underwriters believe can be sold in an orderly manner in such underwritten public offering, then we shall include shares in the offering in accordance with the priority guidelines set forth in the registration rights agreement.

Expenses and Indemnification

Pursuant to the registration rights agreement, we are required to pay all registration expenses, including registration and filing fees, exchange listing fees, printing expenses and accounting fees and the fees and expenses of one counsel to represent the selling stockholders, other than any underwriting discounts and commissions, that are related to any demand or incidental registration described above. The registration rights agreement contains customary cross-indemnification provisions, pursuant to which we are obligated to indemnify the selling stockholders in the event of material misstatements or omissions in the registration statement attributable to us, and the selling stockholders are obligated to provide an undertaking pursuant to which they will indemnify us for material misstatements or omissions in the registration statement attributable to them.

Corporate Opportunity

Our certificate of incorporation provides that the doctrine of "corporate opportunity" will not apply to any of our stockholders or directors, other than in the case of a corporate opportunity that is offered to such person in writing solely in his or her capacity as our director, officer or employee. Accordingly, our stockholders and directors and their respective representatives have no duty to communicate or present corporate opportunities to us and have the right to either hold any corporate opportunity for its (and its representatives') own account and benefit or to recommend, assign or otherwise transfer such corporate opportunity to persons other than us, other than in the case of a corporate opportunity that is offered to such person in writing solely in his or her capacity as our director, officer or employee. As a result, our stockholders, directors and their respective affiliates will not be prohibited from investing in competing businesses or doing business with our customers.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

NASDAQ Global Market Listing

Our common stock is listed on the NASDAQ Global Market under the symbol "BLPH."

Table of Contents

DESCRIPTION OF SECURITIES WE ARE OFFERING

We are offering 17,142,858 Class A Units and 3,000 Class B Units. Class A Units consist of one share of our common stock and a Warrant to purchase one share of our common stock at an exercise price per full share of common stock equal to $0.80. Class B Units consist of one share of our Series A convertible preferred stock, with a stated value of $1,000 per share and convertible into shares of our common stock at the public offering price of the Class A Units, together with the equivalent number of Warrants as would have been issued to such purchaser if they had purchased Class A Units based on the public offering price. The placement agent has informed us that it has not received any indications of interest for Class B Units, thus we do not expect to confirm any sales of such Class B Units. The shares of common stock and Warrant part of a Class A Unit and the Series A convertible preferred stock, and Warrant part of a Class B Unit are each immediately separable and will be issued separately in this offering.

Common Stock

The material terms and provisions of our common stock and each other class of our securities which qualifies or limits our common stock are described under the caption “Description of Capital Stock” in this prospectus.

Series A Convertible Preferred Stock

The following summary of certain terms and provisions of our Series A convertible preferred stock offered in this offering is subject to, and qualified in its entirety by reference to, the terms and provisions set forth in our certificate of designation of preferences, rights and limitations of Series A convertible preferred stock filed as Exhibit 3.3 to the registration statement.

General. Our certificate of incorporation authorizes our Board of Directors to issue up to 5,000,000 shares of our preferred stock, par value $0.01 per share, all of which are undesignated preferred stock.

Subject to the limitations prescribed by our certificate of incorporation, our Board of Directors is authorized to establish the number of shares constituting each series of preferred stock and to fix the designations, powers, preferences and rights of the shares of each of those series and the qualifications, limitations and restrictions of each of those series, all without any further vote or action by our stockholders. Our Board of Directors has designated 12,000 authorized shares of preferred stock as Series A convertible preferred stock. When issued, the shares of Series A convertible preferred stock will be validly issued, fully paid and non-assessable.

Rank. The Series A convertible preferred stock will rank on parity with our common stock and other classes of preferred stock.

Conversion. Each share of the Series A convertible preferred stock is convertible into shares of our common stock (subject to adjustment as provided in the related certificate of designation of preferences, rights and limitations) at any time at the option of the holder at a conversion price equal to the public offering price of the Class A Units, provided that the holder will be prohibited from converting Series A convertible preferred stock into shares of our common stock if, as a result of such conversion, the holder, together with its affiliates, would own more than 4.99% of the total number of shares of our common stock then issued and outstanding. However, any holder may increase or decrease such percentage to any other percentage not in excess of 9.99%, provided that any increase in such percentage shall not be effective until 61 days after such notice to us.

Table of Contents

Voting Rights. Shares of Series A convertible preferred stock will generally have no voting rights, except as required by law and except that the consent of the holders of the majority of the outstanding Series A convertible preferred stock will be required to (a) alter or change adversely the powers, preferences or rights given to the Series A convertible preferred stock or alter or amend the certificate of designation, (b) authorize or create any class of stock ranking as to dividends, redemption or distribution of assets upon a liquidation, dissolution or winding up of the Company, whether voluntary or involuntary, that is senior to the Series A convertible preferred stock, (c) amend our certificate of incorporation or other charter documents in any manner that adversely affects any rights of the holder of the Series A convertible preferred stock, (d) increase the number of authorized shares of the Series A convertible preferred stock, or (e) enter into any agreement with respect to any of the foregoing.

Dividends. Shares of Series A convertible preferred stock will not be entitled to receive any dividends, unless and until specifically declared by our Board of Directors. The holders of the Series A convertible preferred stock will participate, on an as-if-converted-to-common stock basis, in any dividends to the holders of common stock.

Redemption. We are not obligated to redeem or repurchase any shares of Series A convertible preferred stock. Shares of Series A convertible preferred stock are not otherwise entitled to any redemption rights or mandatory sinking fund or analogous fund provisions.

Exchange Listing. We do not plan on making an application to list the Series A convertible preferred stock on The NASDAQ Global Market, any national securities exchange or other nationally recognized trading system. We expect the common stock issuable upon conversion of the Series A convertible preferred stock to be listed on The NASDAQ Global Market.

Warrants to Purchase Common Stock

The material terms of the Warrants to be issued are summarized below. This summary does not purport to be complete in all respects. This description is subject to and qualified entirely by the terms of the form of warrant filed as an exhibit to the registration statement of which this prospectus is a part.

The Warrants to be issued with each unit will have an exercise price per full share of common stock of $0.80 per share and will be immediately exercisable and will expire five years from the date on which such Warrants become exercisable.

The Warrants may not be exercised by the holder to the extent that the holder, together with its affiliates, would beneficially own, after such exercise more than 4.99% of the shares of common stock then outstanding (subject to the right of the holder to increase or decrease such beneficial ownership limitation upon notice to us, provided that such limitation cannot exceed 9.99%) and provided that any increase in the beneficial ownership limitation shall not be effective until 61 days after such notice is delivered.

The Warrants are exercisable for cash or, solely in the absence of an effective registration statement or prospectus, by cashless exercise.

The exercise price of the Warrants is subject to adjustment in the case of stock dividends or other distributions on shares of common stock or any other equity or equity equivalent securities payable in shares of common stock, stock splits, stock combinations, reclassifications or similar events affecting our common stock, and also, subject to limitations, upon any distribution of assets, including cash, stock or other property to our stockholders.

Prior to the exercise of any Warrants, holders of the Warrants will not have any of the rights of holders of the common stock purchasable upon exercise, including voting rights, however, the holders of the Warrants will have certain rights to participate in distributions or dividends paid on our common stock to the extent set forth in the warrants.

In the event of a fundamental transaction, as described in the Warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding common stock, or any person or group becoming the beneficial owner of 50% of the voting power represented by our outstanding common stock, then we will be obligated to purchase the Warrants from the holders thereof concurrently with the consummation of such transaction by paying the holders an amount of cash based on a Black Scholes formula as set forth in the Warrants.

The number of shares of our common stock exercisable, the exercise price or the exercise period of the Warrants may not be amended without the written consent of the holder of each such Warrant.

We do not plan on applying to list the Series A convertible preferred stock or any of the Warrants on the NASDAQ Global Market, any other national securities exchange or any other nationally recognized trading system.

Table of Contents

PLAN OF DISTRIBUTION

Pursuant to an engagement agreement dated October 14, 2016, as amended on November 17, 2016, we have engaged H.C. Wainwright & Co., LLC, or the placement agent, to act as our exclusive placement agent in connection with this offering of our shares of common stock and warrants pursuant to this registration statement and accompanying prospectus. Under the terms of the engagement agreement, the placement agent has agreed to be our exclusive placement agent, on a reasonable best efforts basis, in connection with the issuance and sale by us of our units being offered in this registration statement. The terms of this offering were subject to market conditions and negotiations between us, the placement agent and prospective investors. The engagement agreement does not give rise to any commitment by the placement agent to purchase any of our securities, and the placement agent will have no authority to bind us by virtue of the engagement agreement. Further, the placement agent does not guarantee that it will be able to raise new capital in any prospective offering. The placement agent may engage sub-agents or selected dealers to assist with the offering.

Investors purchasing $100,000 or more of the securities offered hereby will execute a securities purchase agreement with us, providing such investors with certain representations, warranties and covenants from us, which representations, warranties and covenants will not be available to investors of lesser amounts of our securities. Therefore, investors purchasing $100,000 or less of the securities shall rely solely on this prospectus in connection with the purchase of securities in the offering.

We will deliver the units being issued to the investors upon receipt of investor funds for the purchase of the units offered pursuant to this prospectus. We expect to deliver the units being offered pursuant to this prospectus on or about November 29, 2016.

We have agreed to pay the placement agent a total cash fee equal to 7.0% of the gross proceeds of this offering (reduced to 4.0% of the gross proceeds from the sale of securities to entities affiliated with New Mountain Capital, LLC and Linde North America, existing stockholders). We will also reimburse the placement agent (i) $10,000 for its road show expenses and (ii) up to $100,000 for its accountable legal fees and expenses.

Subject to the consummation of this offering, we have also agreed to give the placement agent a 6-month right of first refusal following the consummation of this offering to act as our lead placement agent for any further capital raising transactions undertaken by us; and, in the event that our engagement is terminated without the consummation of this offering, a 6-month tail fee equal to the cash compensation in this offering, if any investor with which we have had substantive discussions with respect to this offering, provides us with further capital during such 6 month period following termination of our engagement.

In addition, pursuant to the terms of the Securities Purchase Agreement, we have agreed for a specified period of time not to sell any shares of common stock or common stock equivalents in a variable rate transaction.

Table of Contents

We have agreed to indemnify the placement agent and specified other persons against some civil liabilities, including liabilities under the Securities Act and the Exchange Act, and to contribute to payments that the placement agent may be required to make in respect of such liabilities.

The placement agent may be deemed to be an underwriter within the meaning of Section 2(a)(11) of the Securities Act, and any commissions received by it and any profit realized on the resale of the securities sold by it while acting as principal might be deemed to be underwriting discounts or commissions under the Securities Act. As an underwriter, the placement agent would be required to comply with the requirements of the Securities Act and the Exchange Act, including, without limitation, Rule 415(a)(4) under the Securities Act and Rule 10b-5 and Regulation M under the Exchange Act. These rules and regulations may limit the timing of purchases and sales of shares of common stock and warrants by the placement agent acting as principal. Under these rules and regulations, the placement agent:

- may not engage in any stabilization activity in connection with our securities; and

- may not bid for or purchase any of our securities or attempt to induce any person to purchase any of our securities, other than as permitted under the Exchange Act, until it has completed its participation in the distribution.

Our common stock is listed on the Nasdaq Global Market under the symbol “BLPH.”

LEGAL MATTERS

The validity of the securities being offered by this prospectus will be passed upon for us by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., New York, New York. The placement agent is being represented by Ellenoff Grossman & Schole LLP.

EXPERTS

The consolidated financial statements of Bellerophon Therapeutics, Inc. (formerly Bellerophon Therapeutics LLC) and subsidiaries as of December 31, 2015 and 2014, and for each of the years in the three-year period ended December 31, 2015, have been incorporated by reference herein in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have filed with the SEC a registration statement on Form S-1, as amended, under the Securities Act, with respect to the securities being offered by this prospectus. 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 securities 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 NE, 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. You may also request a copy of these filings, at no cost, by writing us at 184 Liberty Corner Road, Suite 302, Warren, New Jersey 07059.

We are subject to the information and periodic reporting requirements of the Exchange Act, and we file periodic reports, proxy statements and other information with the SEC. These periodic reports, proxy statements and other information are available for inspection and copying at the public reference room and website of the SEC referred to above. We maintain a website at http://www.bellerophon.com. You may access our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act with the SEC free of charge at our website as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is not incorporated by reference in, and is not part of, this prospectus.

Table of Contents

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus.

We incorporate by reference into this prospectus and the registrations statement of which this prospectus is a part the information or documents listed below that we have filed with the SEC (Commission File No. 001-37544):

- our annual report on Form 10-K for the year ended December 31, 2015, filed with the SEC on March 21, 2016;
- our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 27, 2016 (other than the portions thereof which are furnished and not filed);
- our quarterly reports on Form 10-Q for the quarters ended March 31, 2016, June 30, 2016 and September 30, 2016, filed with the SEC on May 10, 2016, August 9, 2016 and November 8, 2016, respectively;
- our current reports on Form 8-K, filed with the SEC on January 12, 2016, February 18, 2016, February 23, 2016, March 21, 2016, May 10, 2016, May 27, 2016, June 16, 2016, June 17, 2016, July 27, 2016, August 9, 2016, September 20, 2016 (excluding any information deemed furnished pursuant to Item 2.02 or Item 7.01 of any Current Report on Form 8-K) and November 15, 2016; and
- the description of our common stock contained in our registration statement on Form 8-A, filed with the SEC on February 10, 2015, including all amendments and reports filed for the purpose of updating such description.

In addition, all documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, prior to the termination of the offering, shall be deemed to be incorporated by reference into this prospectus.

We will provide to each person, including any beneficial owners, to whom a prospectus is delivered, a copy of any or all of the reports or documents that have been incorporated by reference in the prospectus contained in the registration statement but not delivered with the prospectus. We will provide these reports or documents upon written or oral request at no cost to the requester. You should direct any written requests for documents to Bellerophon Therapeutics, Inc., Attention Investor Relations, 184 Liberty Corner Road, Suite 302, Warren, New Jersey 07059.

In accordance with Rule 412 of the Securities Act, any statement contained in a document incorporated by reference herein shall be deemed modified or superseded to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement.

Table of Contents

17,142,858 Class A Units consisting of Common Stock and Warrants and
3,000 Class B Units consisting of Series A Convertible Preferred Stock and Warrants

(3,529,412 shares of Common Stock underlying the Series A Convertible Preferred Stock)
(17,142,858 shares of Common Stock underlying the Warrants included in the Class A and Class B Units)

PROSPECTUS

H.C. Wainwright & Co.

November 22, 2016