UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2018

or

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

For the transition period from to

Commission file number 001-36845

Bellerophon Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**47-3116175**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
184 Liberty Corner Road, Suite 302 **Warren, New Jersey**	**07059**
(Address of principal executive offices)	(Zip Code)

Registrant's telephone number, including area code: **(908) 574-4770**

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

Title of each class	Name of each exchange on which registered
Common Stock, $0.01 par value per share	**The Nasdaq Global Market**

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

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

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

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

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

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

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

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

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

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

As of June 29, 2018, the aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant was approximately $62.4 million, based upon the closing price on the Nasdaq Global Market reported for such date. Shares of common stock beneficially owned by each officer and director and by each person who is known to own 10% or more of the outstanding common stock have been excluded in that such persons may be

deemed to be affiliates of the registrant. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The number of shares outstanding of the registrant's common stock, as of March 12, 2019: 68,906,765

DOCUMENTS INCORPORATED BY REFERENCE

The following documents (or parts thereof) are incorporated by reference into the following parts of this Form 10-K: Certain information required in Part III of this Annual Report on Form 10-K is incorporated from the registrant's Proxy Statement for the Annual Meeting of Stockholders to be held on May 14, 2019.

TABLE OF CONTENTS

PART I

Item 1.	Business	4
Item 1A.	Risk Factors	31
Item 1B.	Unresolved Staff Comments	65
Item 2.	Properties	65
Item 3.	Legal Proceedings	65
Item 4.	Mine Safety Disclosures	65

PART II

Item 5.	Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities	66
Item 6.	Selected Financial Data	66
Item 7.	Management's Discussion and Analysis of Financial Condition and Results of Operations	68
Item 7A.	Quantitative and Qualitative Disclosures About Market Risk	82
Item 8.	Financial Statements and Supplementary Data	82
Item 9.	Changes in and Disagreements With Accountants on Accounting and Financial Disclosure	104
Item 9A.	Controls and Procedures	104
Item 9B.	Other Information	105

PART III

Item 10.	Directors, Executive Officers and Corporate Governance	106
Item 11.	Executive Compensation	107
Item 12.	Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	108
Item 13.	Certain Relationships and Related Transactions, and Director Independence	108
Item 14.	Principal Accountant Fees and Services	108

PART IV

Item 15.	Exhibits and Financial Statement Schedules	109
Item 16.	Form 10-K Summary	110

REFERENCES TO BELLEROPHON

In this Annual Report on Form 10-K, unless otherwise stated or the context otherwise requires references to the “Company,” “Bellerophon,” “we,” “us” and “our” refer to Bellerophon Therapeutics, Inc. and its consolidated subsidiaries.

FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Annual Report on Form 10-K, including statements regarding our future results of operations and financial position, business strategy and plans and objectives of management for future operations, are forward-looking statements. The words “may,” “will,” “should,” “expects,” “plans,” “anticipates,” “could,” “intends,” “target,” “projects,” “contemplates,” “believes,” “estimates,” “predicts,” “potential” or “continue” or the negative of these terms or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this Annual Report on Form 10-K include, among other things, statements about:

- the timing of the ongoing and expected clinical trials of our product candidates, including statements regarding the timing of completion 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.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the “Risk Factors” section, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

This Annual Report on Form 10-K includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and third-party research,

surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information.

PART I

Item 1. Business

Overview

We are a clinical-stage therapeutics company focused on developing innovative products 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 pulsatile nitric oxide delivery platform, INOpulse.

In 2016, we began developing INOpulse for the treatment of pulmonary hypertension associated with interstitial lung disease (PH-ILD), which includes PH associated with idiopathic pulmonary fibrosis (PH-IPF) as well as other pulmonary fibrosing diseases. During May 2017, we announced the completion of our Phase 2 clinical trial using INOpulse therapy to treat PH-IPF. The clinical data showed that INOpulse was associated with clinically meaningful improvements in hemodynamics and exercise capacity in difficult-to-treat PH-IPF patients. The PH-IPF trial was a proof of concept study (n=4) designed to evaluate the ability of pulsed inhaled nitric oxide, or iNO, to provide selective vasodilation as well as to assess the potential for improvement in hemodynamics and exercise capacity in PH-IPF patients. The clinical trial met its primary endpoint showing an average of 15.3% increase in blood vessel volume ($p<0.001$) during acute inhalation of iNO as well as showing a significant association between ventilation and vasodilation, demonstrating the ability of INOpulse to provide selective vasodilation to the better ventilated areas of the lung. The trial showed consistent benefit in hemodynamics with a clinically meaningful average reduction of 14% in systolic pulmonary arterial pressure (sPAP) with acute exposure to iNO. The study assessed both the iNO 75 and iNO 30 dose, supporting iNO 30 as a potentially safe dose.

During August 2017, we announced acceptance by the U.S. Food and Drug Administration (the "FDA") of our Investigational New Drug (IND) application for our Phase 2b (iNO-PF) clinical trial using INOpulse therapy in a broad population of patients with pulmonary fibrosis, or PF, at both low and intermediate/high risk of PH. In January 2018, we announced the first patient enrollment in our iNO-PF Phase 2b trial. In October 2018, we announced the enrollment completion of the planned 40 subjects, or cohort 1, in our iNO-PF trial. In addition, we announced the expansion of the trial with the addition of cohort 2 and cohort 3, to evaluate a higher iNO 45 and iNO 75 dose as well as a longer 16 week evaluation period. In January 2019, we announced top-line results from cohort 1 of our iNO-PF trial. The results showed statistically significant improvements in multiple clinically meaningful activity parameters as measured by a wearable medical-grade activity monitor: subjects on iNO demonstrated an increase of 8% in moderate activity versus a 26% decrease for subjects on placebo ($p=0.04$) and subjects on iNO showed no decline in their overall activity levels versus a 12% decline for subjects on placebo ($p=0.05$). In addition, clinically meaningful improvements were also demonstrated in the following key areas: subjects on iNO showed an increase of 15% in NT-ProBNP versus a 42% increase for subjects on placebo (NT-ProBNP is a peptide marker of right ventricular failure, with higher levels indicative of disease worsening) and subjects on iNO demonstrated improved oxygen saturation by 9% versus a worsening of 11% for placebo. In addition, iNO was well-tolerated with no safety concerns, supporting the continuation into cohort 2. Actigraphy (medical wearable continuous activity monitoring) provides highly sensitive objective real-world physical activity data that correlates to clinically meaningful patient functional abilities and health outcomes. We are currently utilizing Actigraphy to evaluate multiple clinically meaningful activity parameters in the iNO-PF study. Actigraphy is currently being utilized as the primary endpoint in multiple late-stage clinical programs in various cardiopulmonary diseases such as heart failure and COPD.

We completed a randomized, placebo-controlled, double-blind, dose-confirmation Phase 2 clinical trial of INOpulse for pulmonary hypertension associated with chronic obstructive pulmonary disease, or PH-COPD, in July 2014. The results from this trial showed that iNO 30 was a potentially safe and effective dose for treatment of PH-COPD. Based on the results of this trial, we completed further Phase 2 testing to assess the targeted vasodilation provided by INOpulse in this patient population. We presented the results of this trial in September 2015 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 entitled “Pulmonary vascular effects of pulsed inhaled nitric oxide in COPD patients with pulmonary hypertension.” During September 2017, we shared the results of our Phase 2a PH-COPD trial that was designed to evaluate the acute effects of pulsed inhaled nitric oxide, or iNO, on vasodilation as well as the chronic effect on hemodynamics and exercise tolerance. The trial showed a statistically significant increase (average 4.2%) in blood vessel volume on iNO compared to baseline ($p=0.03$), and a statistically significant correlation in Ventilation-Vasodilation ($p=0.01$). The chronic results demonstrated a statistically significant and clinically meaningful increase in six minute walk distance, or 6MWD, of 50.7m ($p=0.04$) as well as a decrease of 19.9% in systolic pulmonary arterial pressure ($p=0.02$), as compared to baseline. The dose was well tolerated with no related safety concerns. In May 2018, we announced that the FDA concurred with the design of our planned Phase 2b study of INOpulse for treatment of PH-COPD. The study will

assess the effect of INOpulse on various parameters including exercise capacity, right ventricular function and oxygen saturation, as well as other composite endpoints. We are currently evaluating alternatives for the funding and timing of this program.

In 2018, we also initiated development of INOpulse for the treatment of PH associated with Sarcoidosis (PH-Sarc). The study is a Phase 2 dose escalation design that will utilize right heart catheterization to assess the hemodynamic effect of INOpulse from a dose of iNO 30 to iNO 125 in PH-Sarc subjects. We have finalized the design of the study and are in the process of initiating sites, and expect to enroll our first subject in early 2019, with results expected later in 2019.

We initiated a Phase 3 clinical trial of INOpulse for PAH in June 2016. As agreed upon with the FDA, a pre-specified interim analysis was conducted by the Data Monitoring Committee, or DMC, in August 2018, after half of the planned subjects completed 16 weeks of blinded treatment. The data showed INOpulse provided clinically meaningful improvements in pulmonary vascular resistance (18%), cardiac output (0.7 L/min) and NT Pro-BNP. The trial results showed 6 minute walk distance was improved when subjects were on less background therapies and more patients deteriorated in 6MWD on placebo as compared to iNO. In addition, INOpulse was well tolerated and there were no safety concerns. Subjects on PAH background mono-therapy showed a 23 meter improvement in 6MWD, while subjects that were not on prostanoid background therapy showed a 17 meter improvement in 6MWD. However, the DMC determined that the overall change in 6MWD, the primary endpoint of the trial, was insufficient to support the continuation of the study. Accordingly, based on the DMC's recommendation, we discontinued the trial in August 2018.

Other potential indications for our INOpulse platform include: chronic thromboembolic PH, or CTEPH 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 performance of IND-enabling studies, 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 INOpulse and indications for which we have worldwide commercialization rights.

Product	Indication	Stage of Development
INOpulse®	**Indications under development**	
	PH associated with idiopathic pulmonary fibrosis	Phase 2
	PH associated with chronic obstructive pulmonary disease	Phase 2
	PH associated with sarcoidosis	Phase 2
	Additional indications:	
	Pulmonary arterial hypertension	
	Chronic thromboembolic PH	
	PH associated with pulmonary edema from high altitude sickness	

From the inception of our business through December 31, 2018, $282.0 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 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 CTEPH, PH-Sarc 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. In April 2018, we expanded the scope of our license from PH-IPF to PH in patients with Pulmonary Fibrosis (PH-PF), which includes idiopathic interstitial pneumonias, chronic hypersensitivity pneumonitis, occupational and environmental lung disease, with a royalty equal to 1% of net sales of any commercial products for PH-PF.

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 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 that 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 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 previous Phase 2 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 began 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 one or 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 modifications in the INOpulse device. We conducted two studies to assess the environmental and the expiratory concentration of nitrogen dioxide associated with use of the INOpulse delivery system. Both studies found that the nitrogen dioxide levels were below the National Ambient Air Quality Standards.

Our technology is based on patents we have exclusively licensed from Ikaria for the treatment of PAH, PH-COPD, PH-PF, CTEPH, PH-Sarc and PH associated with pulmonary edema from high 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. We have also expanded our patent portfolio by filing several Company-owned patent applications relating to the use of nitric oxide that will expire as late as 2038.

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. This patent was granted by the European Patent Office on March 30, 2016, and was subsequently validated in 30 European countries. Also during January 2016, we received European Conformity, or EC, Certification for our proprietary new, INOpulse® drug-device delivery system. This 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, or the EU. 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 PH-ILD

We are developing INOpulse for the treatment of pulmonary hypertension associated with interstitial lung disease (PH-ILD). Interstitial lung diseases (ILD) is a general category that includes many different lung conditions. All ILDs affect the interstitium, a lace-like network of tissue that extends throughout both lungs. ILDs are a chronic progressive disease of destruction of the airways and lung tissue. This disease results in scarring, thickening of the lung tissue causing insufficient ability for the lungs to oxygenate blood to be delivered to the body, caused by imbalance in mediators and chronic inflammation. While ILD is primarily a respiratory disease, it can also affect the pulmonary vasculature, resulting in vascular remodeling and pulmonary hypertension. Chronic elevation of the pulmonary artery pressures puts stress on the right ventricle and can lead to right ventricular failure.

One of the largest and most serious subsets of ILDs is idiopathic pulmonary fibrosis (IPF), a progressive disease of unknown etiology associated with growth of fibrotic tissue in the lungs causing hypoxemia, dyspnea, fatigue and cough. 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. There are two therapies that are currently approved to treat IPF, Nintedanib and Pirfenidone, each of which costs approximately $100,000 per year. PH with IPF increases mortality, with a median survival of only two to three years. The presence of PH correlates most closely with the need for oxygen therapy. However, there are currently no treatments approved to treat PH associated with IPF.

iNO may improve outcomes in PH-PF including PH-IPF by both improving Ventilation-Perfusion, or V/Q, matching with increases in arterial oxygenation and by lowering pulmonary artery pressures. It has been shown (Yoshida et al., Eur Respir J 1997: 10: 2051-2054) that inhalation of nitric oxide significantly reduced the mean pulmonary arterial pressure and the pulmonary vascular resistance as compared with room air alone in subjects with PH-IPF. In addition, the combined inhalation of nitric oxide and oxygen produced both 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 patients with PH-PF including PH-IPF.

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% (Ford et al., Chest, 2015, Vol 147, pp 31-45).

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. In order to confirm the dose with our proprietary INOpulse device, we conducted a Phase 2 acute dose ranging randomized placebo-controlled trial in 159

patients with the INOpulse DS device, with doses ranging from iNO 3 to iNO 75. 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. 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 subsequent work with acute testing, we 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, and enrolled the first patient in October 2016. During September 2017, we shared the results of our Phase 2a PH-COPD trial that was designed to evaluate the acute effects of iNO on vasodilation as well as the chronic effect on hemodynamics and exercise tolerance. The trial showed a statistically significant increase (average 4.2%) in blood vessel volume on iNO compared to baseline (p=0.03), and a statistically significant correlation in Ventilation-Vasodilation (p=0.01). The chronic results demonstrated a statistically significant and clinically meaningful increase in 6MWD of 50.7m (p=0.04) as well as a decrease of 19.9% in systolic pulmonary arterial pressure (p=0.02), as compared to baseline. In May 2018, we announced that the FDA concurred with the design of our planned Phase 2b trial of INOpulse for treatment of PH-COPD. The study will assess the effect of INOpulse on various parameters, including exercise capacity, right ventricular function and oxygen saturation, as well as other composite endpoints. We are currently evaluating alternatives for the funding and timing of this program.

INOpulse for PH-Sarcoidosis

In 2018, we also initiated development of INOpulse for the treatment of PH associated with Sarcoidosis (PH-Sarc). The study is a Phase 2a dose escalation design that will utilize right heart catheterization to assess the hemodynamic effect of INOpulse from a dose of iNO 30 to iNO 125 in PH-Sarc subjects. We have finalized the design of the trial and are in the process of initiating sites, and expect to enroll our first subject in early 2019, with results expected later in 2019.

INOpulse for PAH

PAH is characterized by abnormal constriction and remodeling 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. PAH affects fewer than 200,000 individuals in the United States and 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 reinforced the results from October 2014 and indicated a sustainability of benefit to PAH patients who received INOpulse therapy at the 75 mcg/kg 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 the EMA, on our Phase 3 protocol, we initiated the first of the two Phase 3 trials. In September 2015, the FDA agreed to a special protocol assessment, or SPA, for our Phase 3 PAH program for INOpulse, which will include two confirmatory clinical trials. The INOvation-1 trial was initiated with the first patient enrolled in June 2016. During January 2017, we received confirmation from the FDA of its acceptance of all modifications proposed by us to our Phase 3 program. Under the newly modified Phase 3 program, the ongoing one-year INOvation-1 trial, and a second confirmatory randomized withdrawal study with approximately 40 patients who will be crossing over from the INOvation-1 trial, can serve as the two adequate and well-controlled clinical trials to support an NDA submission for INOpulse in PAH subjects on LTOT. As agreed upon with the FDA, a pre-specified interim analysis was conducted by the Data Monitoring Committee, or DMC, in August 2018, after half of the planned subjects completed 16 weeks of blinded treatment. The data showed INOpulse provided clinically meaningful improvements in pulmonary vascular resistance (18%), cardiac output (0.7 L/min) and NT Pro-BNP. In addition, subjects on PAH background

mono-therapy showed a 23 meter improvement in 6MWD, while subjects who were not on prostanoid background therapy showed a 17 meter improvement in 6MWD. However, the DMC determined that the overall change in 6MWD, the primary endpoint of the trial, was insufficient to support the continuation of the study. Accordingly, based on the DMC's recommendation, we discontinued the trial in August 2018. The trial results showed 6MWD was improved when subjects were on less background therapies and more patients deteriorated in 6MWD on placebo as compared to iNO. In addition, INOpulse was well tolerated and there were no safety concerns.

BCM

In December 2011, we initiated a clinical trial of Bioabsorbable Cardiac Matrix, or BCM, and completed enrollment in December 2014. Top-line results from the clinical trial were announced in July 2015. In July 2018, we informed BioLineRx Ltd., from whom we in-licensed the BCM technology, of our decision to discontinue further development and terminate the License and Commercialization Agreement.

Our Strategy

Our goal is to become a leader in developing and commercializing innovative products 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 PH-ILD. Our Phase 2b PH-PF program for INOpulse includes 80 patients in three cohorts to evaluate different doses of iNO for periods of eight to 16 weeks. We also completed Phase 2 studies for INOpulse in PH-COPD looking at the effect of chronic use on exercise capacity and initiated a Phase 2 dose escalation study for PH-Sarc.

- *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 and PH associated with pulmonary edema from high 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 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 2018. 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, 3 and 5 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. 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-ILD, among others. Group 5 PH consists of PH associated with blood, systematic and metabolic disorders. This Group includes patients with PH-Sarc.

INOpulse for PH-ILD

We are developing INOpulse for the treatment of pulmonary hypertension associated with interstitial lung disease (PH-ILD). Interstitial lung diseases (ILD) is a general category that includes many different lung conditions. All ILDs affect the interstitium, a lace-like network of tissue that extends throughout both lungs. ILDs are a chronic progressive disease of destruction of the airways and lung tissue. This disease results in scarring, thickening of the lung tissue causing insufficient ability for the lungs to oxygenate blood to be delivered to the body, caused by imbalance in mediators and chronic inflammation. While ILD is primarily a respiratory disease, it can also affect the pulmonary vasculature, resulting in vascular remodeling and pulmonary hypertension. Chronic elevation of the pulmonary artery pressures puts stress on the right ventricle and can lead to right ventricular failure.

Disease Background and Market Opportunity

One of the largest and most serious subsets of ILDs is idiopathic pulmonary fibrosis (IPF), a progressive disease of unknown etiology associated with growth of fibrotic tissue in the lungs causing hypoxemia, dyspnea, fatigue and cough. 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. There are two therapies that are currently approved to treat IPF, Nintedanib and Pirfenidone, each of which costs approximately $100,000 per year. PH with IPF increases mortality, with a median survival of only two to three years. The presence of PH correlates most closely with the need for oxygen therapy. However, there are currently no treatments approved to treat PH associated with IPF.

Scientific Rationale for Use of INOpulse for PH-ILD

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-ILD.

iNO may also improve outcomes in PH-PF including PH-IPF by both improving Ventilation-Perfusion, or V/Q, matching with increases in arterial oxygenation and by lowering pulmonary artery pressures. It has been shown (Yoshida et al., Eur Respir J 1997: 10: 2051-2054) that inhalation of nitric oxide significantly reduced the mean pulmonary arterial pressure and the pulmonary vascular resistance as compared with room air alone in PH-IPF. However, the arterial oxygen partial pressure (PaO2) did not improve. The combined inhalation of nitric oxide and oxygen produced both 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 patients with PH-PF including PH-IPF.

Clinical Development Program

During May 2017, we announced the completion of our Phase 2 clinical trial using INOpulse therapy to treat PH-IPF. The clinical data showed that INOpulse was associated with clinically meaningful improvements in hemodynamics and exercise capacity in difficult-to-treat PH-IPF patients. The PH-IPF trial was a proof of concept study (n=4) designed to evaluate the ability of pulsed inhaled nitric oxide, or iNO, to provide selective vasodilation as well as to assess the potential for improvement in hemodynamics and exercise capacity in PH-IPF patients. The clinical trial met its primary endpoint showing an average of 15.3% increase in blood vessel volume ($p<0.001$) during acute inhalation of iNO as well as showing a significant association between ventilation and vasodilation, demonstrating the ability of INOpulse to provide selective vasodilation to the better ventilated areas of the lung. The trial showed consistent benefit in hemodynamics with a clinically meaningful average reduction of 14% in systolic pulmonary arterial pressure (sPAP) with acute exposure to iNO, and assessed both the iNO 75 and iNO 30 dose, supporting iNO 30 as a potentially safe dose.

During August 2017, we announced FDA acceptance of our IND for our Phase 2b (iNO-PF) clinical trial using INOpulse therapy in a broad population of patients with pulmonary fibrosis, or PF, at both low and intermediate/high risk of PH. In January 2018, we announced the first patient enrollment in our iNO-PF Phase 2b trial. In October 2018, we announced the enrollment completion of the planned 40 subjects, or cohort 1, in our iNO-PF trial. In addition, we announced the expansion of the trial with the addition of two cohorts:

- Cohort 2 - randomized, placebo-controlled, double-blind clinical trial with patients randomized 2:1 to iNO45 (45 mcg/kg ideal body weight/hour) or to placebo, for 16 weeks.
- Cohort 3 - randomized, placebo-controlled, double-blind clinical trial with patients randomized 2:1 to iNO75 (75 mcg/kg ideal body weight/hour) or to placebo, for 16 weeks.

In addition, we also added a dose escalation trial from iNO 45 to iNO 75 as part of our open label extension program.

In January 2019, we announced top-line results from cohort 1 of our iNO-PF study. The results showed statistically significant improvements in multiple clinically meaningful activity parameters as measured by a wearable medical-grade activity monitor: subjects on iNO demonstrated an increase of 8% in moderate activity versus a 26% decrease for subjects on placebo ($p=0.04$) and subjects on iNO showed no decline in their overall activity levels versus a 12% decline for subjects on placebo ($p=0.05$). In addition, clinically meaningful improvements were also demonstrated in the following key areas: subjects on iNO showed an increase of 15% in NT-ProBNP versus a 42% increase for subjects on placebo (NT-ProBNP is a peptide marker of right ventricular failure, with higher levels indicative of disease worsening) and subjects on iNO demonstrated improved oxygen saturation by 9% versus a worsening of 11% for placebo. In addition, iNO was well-tolerated with no safety concerns supporting the continuation into cohort 2. Actigraphy (medical wearable continuous activity monitoring) provides highly sensitive objective real-world physical activity data that correlates to clinically meaningful patient functional abilities and health outcomes. We are currently utilizing actigraphy to evaluate multiple clinically meaningful activity parameters in the iNO-PF study. Actigraphy is currently being utilized as the primary endpoint in multiple late-stage clinical programs in various cardiopulmonary diseases such as heart failure and COPD.

In 2018, we also implemented a dose escalation design which will utilize right heart catheterization to assess the hemodynamic effect of INOpulse from a dose of iNO 30 to iNO 125 in PH-ILD subjects.

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 the 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 extent of the chronic pulmonary pathology impairs gas exchange resulting in deprivation of adequate oxygen supply, or hypoxia, and 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 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, and are 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 PH-ILD. 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 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. 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 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. During September 2017, we shared the results of our Phase 2a PH-COPD study designed to evaluate the acute effects of pulsed inhaled nitric oxide, or iNO, on vasodilation as well as the chronic effect on hemodynamics and exercise tolerance. In May 2018, we announced that we reached agreement with the FDA on the design of our planned Phase 2b study of INOpulse for treatment of PH-COPD. The study will assess the effect of INOpulse on various parameters including exercise capacity, right ventricular function, oxygen saturation as well as other composite endpoints. We are currently evaluating alternatives for the funding and timing of this program.

INOpulse for PH-Sarcoidosis

We are also developing INOpulse for PH-Sarcoidosis. We believe the mechanism of action of inhaled nitric oxide as a targeted pulmonary vasodilator, and thus INOpulse, can be effective in treating PH related to other conditions including PH associated with sarcoidosis. Sarcoidosis is a multi-system disease which is characterized by the growth of granulomas (inflammatory cells) in one or more organs. The most frequent organs involved are the lungs and lymph nodes within the chest. Pulmonary hypertension may be present in as many as 74% of patients depending on how the pulmonary hypertension (PH) is defined. The presence of PH in sarcoidosis is associated with a poor prognosis. There are a number of different mechanisms linking PH with sarcoidosis. The primary treatment for sarcoidosis is corticosteroids; however, the outcome of this treatment on the PH is unclear. There is no approved therapy for PH associated with sarcoidosis. Various PAH treatments have been tried including iNO and IV prostacyclin with some clinical and functional improvement.

In 2018, we also initiated development of INOpulse for the treatment of PH associated with Sarcoidosis (PH-Sarc). The study is a Phase 2 dose escalation design that will utilize right heart catheterization to assess the hemodynamic effect of INOpulse from a dose of iNO 30 to iNO 125 in PH-Sarc subjects. We have finalizedm the design of the study and are in the process of initiating sites, and expect to enroll our first subject in early 2019, with results expected later in 2019.

INOpulse for Pulmonary Arterial Hypertension

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. 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.

Clinical Development Program

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 reinforced the results from October 2014 and indicated 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 EMA on our Phase 3 protocol, we initiated the first of the two Phase 3 trials. In September 2015, the FDA agreed to a SPA for our Phase 3 PAH program for INOpulse, which will include two confirmatory clinical trials. The INOvation-1 trial was initiated with the first patient enrolled in June 2016. During January 2017, we received confirmation from the FDA of its acceptance of all modifications proposed by us to our Phase 3 program. Under the newly modified Phase 3 program, the ongoing one-year INOvation-1 trial, and a second confirmatory randomized withdrawal study with approximately 40 patients who will be crossing over from the INOvation-1 trial, can serve as the two adequate and well-controlled trials to support a NDA filing for INOpulse in PAH subjects on LTOT. As agreed upon with the FDA, a pre-specified interim analysis was conducted by the Data Monitoring Committee, or DMC, in August 2018, after half of the planned subjects completed 16 weeks of blinded treatment. The data showed INOpulse provided clinically meaningful improvements in pulmonary vascular resistance (18%), cardiac output (0.7 L/min) and NT Pro-BNP. In addition, subjects on PAH background mono-therapy showed a 23 meter improvement in 6MWD, while subjects that were not on prostanoid background therapy showed a 17 meter improvement in 6MWD. However, the DMC determined that the overall change in 6MWD, the primary endpoint of the trial, was insufficient to support the continuation of the study. Accordingly, based on the DMC's recommendation, we have discontinued the trial. The trial results showed 6MWD was improved when subjects were on less background therapies and more patients deteriorated in 6MWD on placebo as compared to iNO. In addition, INOpulse was well tolerated and there were no safety concerns.

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 and PH-ILD are classified under Group 3, PH due to lung disease and/or hypoxemia. Group 5 PH consists of PH associated with blood, systematic and metabolic disorders. This Group includes patients with PH-Sarc. We believe the mechanism of action of inhaled nitric oxide as a targeted pulmonary vasodilator, and thus INOpulse, can be effective in treating PH related to other conditions, including CTEPH and PH associated with pulmonary edema from high altitude sickness.

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 the 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.

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 and 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. In July 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.

In April 2018, we expanded the scope of our license from PH-IPF to PH in patients with Pulmonary Fibrosis (PH-PF), which includes idiopathic interstitial pneumonias, chronic hypersensitivity pneumonitis, occupational and environmental lung disease, with a royalty equal to 1% of net sales of any commercial products for PH-PF.

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.

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 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.

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.

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 in the

world for manufacturing medical nitric oxide.

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.

PH 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 PAH Phase 2 trial and Phase 2 PH-PF trial, all patients were tested for rebound PH and we found no adjudicated cases of rebound PH with this testing. Though the likelihood of rebound PH is very low, all of our patients with PAH are currently 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 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. Currently, there are no approved therapies for treating PH-PF including PH-IPF and we are not aware of any therapies 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 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 December 31, 2018, we hold exclusive licenses from Ikaria to at least 100 patents and pending patent applications in both the United States and foreign countries including Australia, Brazil, Canada, China, Eurasia, Europe, Hong Kong, India, Indonesia, Israel, Japan, Korea, Mexico, the Philippines, Russia, Singapore and South Africa. 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, Canada, China, Europe, Hong Kong, Japan and Mexico. Patent applications are pending in Australia, Brazil, Europe, Mexico and the United States. This patent family expires as late as 2027 in the United States and in 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 five issued U.S. patents and issued patents in Australia, Europe, and China, as well as pending applications in the United States as well as Australia, Brazil, Canada, China, Eurasia, Europe, Hong Kong, Israel, India, Japan, Korea, Mexico and South Africa. 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 at least one issued patent in each of the United States, Australia, China, Europe, Hong Kong, Indonesia, Israel, Japan, Korea, Mexico, the Philippines, Russia and Singapore, as well as pending patent applications in the United States, Brazil, Canada, Europe, Hong Kong, India, Israel, Japan, Mexico, 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, design patents covering the ornamental designs of the intended commercial device and clinical device have been granted. We have also filed several Company-owned patent applications relating to the use of nitric oxide.

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.

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 Annual Report on Form 10-K 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 Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with applicable 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 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, 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 in the United States must typically undertake the following:

- completion of pre-clinical laboratory tests, animal studies and formulation studies in compliance with applicable good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, 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 an NDA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is 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; and
- FDA review and approval of the NDA.

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 FDA regulations, including GLP regulations. An IND sponsor must submit the results of the pre-clinical studies, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, to the FDA as part of an IND. Some long-term pre-clinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to the proposed clinical trial and places the IND on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

After the IND becomes effective, the sponsor continues to perform nonclinical studies including those related to the development of a manufacturing process that is capable of consistently producing quality batches of the drug candidate and, the development of 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 support the eventual shelf life and storage of the drug.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written 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 phase of a clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

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.

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.

- Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to 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 serious adverse effects, or 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 and post information about the trial on the National Institutes of Health's ClinicalTrials.gov website.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on two full, or pivotal, 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 and effective and relied upon by the applicant "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 submitted 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 appropriate, the applicant may eliminate the need to conduct certain pre-clinical studies or clinical trials of the new product. The FDA may also require companies to perform additional studies to support any differences 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 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 candidate for one or more indications. Under federal law, the submission of most NDAs is additionally subject to a user fee, which for FY2019 exceeds $2.6 million for NDAs that require clinical trials, and the sponsor of an approved NDA is also subject to annual program fee of $309,915. 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 will be filed because it 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 manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving 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. 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 when making decisions.

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 for approval. If the trials were the subject of discussion at an end-of-Phase 2 meeting with the FDA, an SPA, may be requested for clinical protocols for Phase 3 trials whose data is intended to form the primary basis for an efficacy claim. 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 an 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.

Expedited Review and Approval

The FDA has various programs, including Fast Track, priority review, and accelerated approval, which are intended to expedite or simplify the process for reviewing drugs, and/or provide for approval on the basis of surrogate endpoints. Even if a drug qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification or that the time period for FDA review or approval will not be shortened. Generally, drugs that may be eligible for these programs are those for serious or life threatening conditions, those with the potential to address unmet medical needs, and those that offer meaningful benefits over existing treatments. For example, Fast Track is a process designed to facilitate the development, and expedite the review, of drugs to treat serious diseases and fill an unmet medical need. The request may be made at the time of IND submission and generally no later than the pre NDA meeting. The FDA will respond within 60 calendar days of receipt of the request. Priority review, which is requested at the time of NDA submission, is designed to give drugs that offer major advances in treatment or provide a treatment where no adequate therapy exists an initial review within six months as compared to a standard review time of ten months. Although Fast Track and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast Track designated drug and expedite review of the application for a drug designated for priority review. Accelerated approval provides an earlier

approval of drugs to treat serious diseases, and that fill an unmet medical need based on a surrogate endpoint, which is a laboratory measurement or physical sign used as an indirect or substitute measurement representing a clinically meaningful outcome. Discussions with the FDA about the feasibility of an accelerated approval typically begin early in the development of the drug in order to identify, among other things, an appropriate endpoint. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform post marketing clinical trials to confirm the appropriateness of the surrogate marker trial.

In the Food and Drug Administration Safety and Improvement Act, or FDASIA, Congress encouraged the FDA to utilize innovative and flexible approaches to the assessment of products under accelerated approval. The law required the FDA to issue related draft guidance within a year after the law's enactment and also promulgate confirming regulatory changes. The FDA published a final guidance on May 30, 2014, entitled "Expedited Programs for Serious Conditions-Drugs and Biologics." One of the expedited programs added by FDASIA is that for Breakthrough Therapy. A Breakthrough Therapy designation is designed to expedite the development and review of drugs that are intended to treat a serious condition where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s). A sponsor may request Breakthrough Therapy designation at the time that the IND is submitted, or no later than at the end of Phase II meeting. The FDA will respond to a Breakthrough Therapy designation request within sixty days of receipt of the request. A drug that receives Breakthrough Therapy designation is eligible for all fast track designation features, intensive guidance on an efficient drug development program, beginning as early as Phase I and commitment from the FDA involving senior managers. The FDA has designated over 250 drugs as breakthrough therapies (some were subsequently withdrawn), and over 130 original or supplemental applications with breakthrough designations have been approved to date.

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 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 risk evaluation and mitigation strategy, or 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 some state agencies, and are subject to periodic unannounced inspections by the FDA for compliance with cGMP and other requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. Compliance with cGMPs requires, among other things, the investigation and correction of any deviations from cGMP and the imposition of reporting and documentation requirements upon the sponsor and the manufacturer. 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 the 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;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

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

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, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product). A company must request orphan product designation before submitting an NDA. If the request is granted, the 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 the 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 Best Pharmaceuticals for Children Act, or BPCA, certain drugs may obtain an additional six months of exclusivity, if the sponsor submits information requested in writing by the FDA (a Written Request), relating to the use of the active moiety of the drug in children. The FDA may not issue a Written Request for studies on unapproved or approved indications or where it determines that information relating to the use of a drug in a pediatric population, or part of the pediatric population, may not produce health benefits in that population.

In addition, the Pediatric Research Equity Act, or PREA, requires a sponsor to conduct pediatric studies for most drugs and biologics, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs, biologics license application and supplements thereto, must contain a pediatric assessment unless the sponsor has received a deferral or waiver. Unless otherwise required by regulation, PREA does not apply to any drug for an indication where orphan designation has been granted. The required assessment must assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or the FDA may request a deferral of pediatric studies for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug or biologic is ready for approval for use in adults before pediatric studies are complete or that additional safety or effectiveness data needs to be collected before the pediatric studies begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

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.

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 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 (and supplemental PMAs) 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
- 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.

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 subject to different regulatory requirements, 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 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.

Rest of World Government Regulation

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 and among 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.

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 EU, 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 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 EU 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. EU 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

If our product candidates are approved, we will be subject to federal and state fraud and abuse and other healthcare laws and regulations, which 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;
- we may be subject to, or may in the future become subject to, U.S. federal and state, and foreign laws and regulations imposing obligations on how we collect, use, disclose, store and process personal information. Our actual or perceived failure to comply with such obligations could result in liability or reputational harm and could harm our

business. Ensuring compliance with such laws could also impair our efforts to maintain and expand our customer base and thereby decrease our future revenues;

- 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 ACA 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

- other state and foreign laws and regulations may apply to us.

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.

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 December 31, 2018, we had 17 full-time employees, of which 12 employees were engaged in research and development and five employees provided general and administrative support. Of our employees, eight have earned advanced degrees. Our employees are not represented by a labor union or covered by a collective bargaining agreement.

Our 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 Annual Report on Form 10-K. We have included our website address in this Annual Report on Form 10-K 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.

Available Information

We make available free of charge through our website our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to such reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act. We make these reports available through our website as soon as reasonably practicable after we electronically file or furnish such reports to, the Securities and Exchange Commission, or the SEC. We also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. The information contained on, or that can be access through, our website is not a part of or incorporated by reference in this Annual Report on Form 10-K.

Item 1A. Risk Factors

The following risk factors and other information included in this Annual Report on Form 10-K should be carefully considered. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see page 2 of this Annual Report on Form 10-K for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to Our Financial Position and Need for Additional Capital

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

Since inception, we have incurred significant operating losses. Our net loss was approximately $23.8 million, $54.8 million and $2.8 million for the years ended December 31, 2016, 2017 and 2018, respectively. We do not know whether or when we will become profitable. We have not generated any revenues to date from product sales. We have not completed development of any product candidate and have devoted substantially all of our financial resources and efforts to research and development, including pre-clinical studies and clinical trials. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our deficit and working capital. We anticipate that our expenses will increase substantially if and as we:

- continue our research and clinical development of our product candidates;
- identify, develop and/or in-license additional product candidates;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- in the future, establish a manufacturing, sales, marketing and distribution infrastructure;
- maintain, expand and protect our intellectual property portfolio;
- add equipment and physical infrastructure to support our research and development;
- hire additional clinical, regulatory, quality control and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and any future commercialization efforts.

To become and remain profitable, we must succeed in developing and eventually commercializing products that generate significant revenue. We do not expect to generate significant revenue unless and until we are able to obtain marketing approval for, and successfully commercialize, one or more of our product candidates. This will require us to be successful in a range of challenging activities, including completing pre-clinical studies and clinical trials of our product candidates, discovering additional product candidates, obtaining regulatory approval for our product candidates, manufacturing, marketing and selling any products for which we may obtain regulatory approval, satisfying any post-marketing requirements and obtaining reimbursement for our products from private insurance or government payors. We are in the early stages of most of these activities and have not yet commenced the other activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. If we are required by the FDA or the EMA to perform trials in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates, our expenses could increase.

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

In addition, our recurring losses from operations, accumulated deficit and our need to raise additional financing in order to continue to fund our operations, may raise substantial doubt about our ability to continue as a going concern. Given our planned expenditures for the next several years, including, without limitation, expenditures in connection with our clinical trials, we and our independent registered public accounting firm may conclude that there is substantial doubt regarding our ability to continue as a going concern.

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

We were formed as a wholly-owned subsidiary of Ikaria in October 2013 and became a stand-alone company in February 2014 following the Spin-Out and, as such, have a limited independent operating history.

Our operations to date have been limited to organizing and staffing our company, developing and securing our technology, and undertaking pre-clinical studies and clinical trials of our product candidates. We have not yet demonstrated the ability to complete the development of any product candidates, obtain marketing approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, any predictions our stockholders make about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing products.

Assuming we obtain marketing approval for any of our product candidates, we will need to transition from a company with a research and development focus to a company capable of supporting commercial activities or we will need to enter into strategic partnerships. We may encounter unforeseen expenses, difficulties, complications and delays and may not be successful in such a transition.

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.

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue research and development and initiate additional clinical trials of our product candidates and seek regulatory approval for these and potentially other product candidates. In addition, if we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. In particular, the costs that may be required for the manufacture of any product candidate that receives marketing approval may be substantial. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We plan to use our current cash and cash equivalents and marketable securities primarily to fund our ongoing research and development efforts. We will be required to expend significant funds in order to advance development of our product candidates and any other potential product candidates. Our existing cash and cash equivalents and marketable securities will be used primarily to complete the ongoing Phase 2b trial of INOpulse for PH-ILD and to complete the dose escalation study for PH-Sarc, and will not be sufficient to fund all of the efforts that we plan to undertake or the completion of clinical development or commercialization of any of our product candidates. Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations or licensing arrangements or other sources. Adequate additional funding may not be available to us on acceptable terms or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy.

We believe that our existing cash and cash equivalents as of December 31, 2018, the proceeds from our January 2019 public offering and proceeds that will become available to us upon sale of our state net operating losses and R&D tax credits under the State of New Jersey's Technology Business Tax Certificate Transfer Program will be sufficient to satisfy our operating cash needs for at least one year after the filing of this Annual Report on Form 10-K. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect.

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

- the timing, progress, and results of our ongoing and planned clinical trials of our product candidates;

- our ability to manufacture sufficient clinical supply of our products candidates and the costs thereof;
- discussions with regulatory agencies regarding the design and conduct of our clinical trials and the costs, timing and outcome of regulatory review of our product candidates;
- the cost and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the costs of any other product candidates or technologies we pursue;
- our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;
- the revenue, if any, received from commercial sales of any product candidates for which we receive marketing approval; and
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims.

Identifying potential product candidates and conducting clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for several years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. We also have certain restrictions on issuing shares and incurring indebtedness that are part of our Stockholders Agreement.

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.

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

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of public or private equity offerings, debt financings and/or license and development agreements with collaboration partners. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our stockholders may be materially diluted, and the terms of such securities could include liquidation or other preferences or other rights such as anti-dilution rights that adversely affect the rights of our stockholders. For example, there could be potential dilution from the exercising of the warrants issued in connection with our secondary offering completed in November 2016. Debt financing and preferred equity financing, if available, may involve agreements that include restrictive covenants that limit our ability to take specified actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay,

limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. If we raise funds through collaborations, strategic partnerships or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us.

Risks Related to Our Business and Industry

We face substantial competition from other pharmaceutical, biotechnology and medical device companies and our operating results may suffer if we fail to compete effectively.

The pharmaceutical, biotechnology and medical device industries are highly competitive. There are many pharmaceutical, biotechnology and medical device companies, public and private universities and research organizations actively engaged in the research and development of products that may be similar to our product candidates. In addition, other companies are increasingly looking at the cardiopulmonary disease market as a potential opportunity. For example, currently, there are 14 drugs approved for the treatment of PAH and there are also other potential therapies in clinical development, including other nitric oxide generation and delivery systems.

Many of our competitors, either alone or through their strategic partners, have substantially greater name recognition and financial, technical, manufacturing, marketing and human resources than we do and significantly greater experience and infrastructure in the research and clinical development of medical products, obtaining FDA and other regulatory approvals of those products, and commercializing those products around the world. Additional mergers and acquisitions in the pharmaceutical, biotechnology and medical device industries may result in even more resources being concentrated in our competitors. Large pharmaceutical and medical device companies in particular have extensive expertise in pre-clinical and clinical testing and in obtaining regulatory approvals for medical products. In addition, academic institutions, government agencies and other public and private organizations conducting research may seek patent protection with respect to potentially competitive products or technologies. These organizations may also establish exclusive collaborative or licensing relationships with our competitors. Accordingly, our competitors may be more successful than we may be in obtaining approval for inhaled nitric oxide products and achieving widespread market acceptance. We anticipate that we will face intense and increasing competition as new products and technologies become available.

We will not be able to compete effectively unless we successfully:

- design, develop and commercialize products that are competitive in the market;
- attract qualified scientific, medical, sales and marketing, engineering and commercial personnel;
- obtain patent and/or other proprietary protection for our processes and product candidates; and
- obtain required regulatory approvals.

It is also possible that Ikaria will seek to develop and commercialize inhaled nitric oxide products or product candidates in the Bellerophon indications. While a subsidiary of Ikaria has granted to us an exclusive license to develop and commercialize pulsed nitric oxide in the Bellerophon indications and the scope of that license includes certain technology developed or acquired by that subsidiary after the date of the license agreement, the license does not include technology developed or acquired by other subsidiaries or affiliates of Ikaria including Mallinckrodt's other subsidiaries. Because Ikaria, Mallinckrodt and its other subsidiaries and affiliates are not subject to any non-competition obligations in our favor, it is possible that these other subsidiaries or affiliates of Ikaria or Mallinckrodt may seek to develop or commercialize inhaled nitric oxide or other products or product candidates, using technology not exclusively licensed to us that are competitive with our products or product candidates, which could adversely affect our business, financial condition or results of operations.

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

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 currently have no products approved for sale and have invested a significant portion of our efforts and financial resources in the development of our INOpulse for PAH, INOpulse for PH-ILD, INOpulse for PH-COPD, INOpulse for PH-Sarc and Bioabsorbable Cardiac Matrix, or BCM, product candidates. Our prospects are substantially dependent on our ability to develop, obtain marketing approval for and successfully commercialize these product candidates.

In July 2015, we announced top-line results of our 303-patient, randomized, double-blind, placebo-controlled clinical trial of BCM, which showed no statistically significant treatment differences between patients treated with BCM and patients treated with placebo for both the primary and secondary endpoints. In July 2018, we informed BioLineRx Ltd., from whom we in-licensed the BCM technology, of our decision to discontinue further development and terminate the License and Commercialization Agreement. As a result, we have become even more dependent on the success of our INOpulse product candidates and our ability to develop, obtain marketing approval for and successfully commercialize our INOpulse product candidates.

The success of our product candidates will depend on, among other things, our ability to successfully complete clinical trials of each product candidate. The clinical trial process is uncertain, and failure of one or more clinical trials can occur at any stage of testing. For example, although we believe our Phase 2 clinical trial of INOpulse for PH-COPD supports advancement into further Phase 2 testing, the primary endpoint for INOpulse for PH-COPD was not statistically significant for any of the doses tested.

In addition to the successful completion of clinical trials, the success of our product candidates will also depend on several other factors, including the following:

- receipt of marketing approvals from the FDA or other applicable regulatory authorities;
- establishment of supply arrangements with third-party raw materials suppliers and manufacturers;
- establishment of arrangements with third-party manufacturers to obtain finished drug products that are appropriately packaged for sale;
- the performance of our future collaborators for one or more of our product candidates, if any;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- obtaining and maintaining patent, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- protection of our rights in our intellectual property portfolio;
- launch of commercial sales if and when our product candidates are approved;
- a continued acceptable safety profile of our product candidates following any marketing approval;
- commercial acceptance, if and when approved, by patients, the medical community and third-party payors;
- establishing and maintaining pricing sufficient to realize a meaningful return on our investment; and
- competition with other products.

If we are unable to develop, obtain marketing approval for or successfully commercialize our INOpulse product candidates, either alone or through a collaboration, or experience significant delays in doing so, our business could be materially harmed.

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.

The risk of failure of all of our product candidates is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must conduct extensive clinical trials to demonstrate the safety

and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The clinical development of our product candidates is susceptible to the risk of failure inherent at any stage of development, including failure to demonstrate efficacy in a clinical trial or across a broad population of patients, the occurrence of severe or medically or commercially unacceptable adverse events, failure to comply with protocols or applicable regulatory requirements and determination by the FDA or any comparable non-U.S. regulatory authority that a drug product is not approvable.

It is possible that even if one or more of our product candidates has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any. Similarly, in our clinical trials we may fail to detect toxicity of or intolerability caused by our product candidates, or mistakenly believe that our product candidates are toxic or not well tolerated when that is not in fact the case. Also, the exclusion criteria we define may not sufficiently rule out patients who are at a higher risk of being harmed by the treatment. For example, our exclusion criteria for pre-existing left heart dysfunction in our Phase 2 INOpulse clinical trials completed in 2014 may not rule out patients who may experience an adverse event related to left ventricular function due to exposure to nitric oxide. In addition, patients who are not excluded for reactive pulmonary vasculature when exposed to nitric oxide may still experience PH.

The outcome of pre-clinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results, particularly when earlier trials are small, open-label or non-placebo-controlled trials and in trials that have different endpoints than earlier trials. For example, for BCM, we were using the results of the 27-patient pilot trial conducted by BioLineRx Ltd. that used anatomical changes to measure efficacy and did not have a control group as support for our larger ongoing clinical trial, which did not achieve the same results as the BioLineRx Ltd. trial. Many companies in the biotechnology, pharmaceutical and medical device industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we cannot be certain that we will not face such setbacks.

The design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced or completed. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. In addition, pre-clinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in pre-clinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we believe that the results of clinical trials for our product candidates warrant marketing approval, the FDA or comparable non-U.S. regulatory authorities may disagree and may not grant marketing approval of our product candidates.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants. Any Phase 3 or other clinical trials that we may conduct may not demonstrate the efficacy and safety necessary to obtain regulatory approval to market our product candidates.

INOpulse is a sophisticated electro-mechanical device comprised of components that may fail or deteriorate over time or with improper use. If we experience problems with, failure of, or delays in obtaining any INOpulse components, our business could be materially adversely harmed.

Because INOpulse is a sophisticated electro-mechanical device, the parts which comprise the device are subject to sudden failure or to wear and tear, which may result in decreased function or failure of those parts over time. Although we perform scheduled, preventive maintenance on our drug delivery system to limit device failures, and additional maintenance as needed whenever a user reports a device malfunction, components of our devices may fail. In addition, although we have designed INOpulse to be simple and easy to use and will provide user manuals and other training materials, users of INOpulse may use the devices improperly, which could cause the devices to fail or otherwise not work properly.

There are several components in INOpulse that are custom designed or assembled for us. We are dependent on a single company to supply us with some of these components. While we believe there are alternative suppliers from which we could purchase most of these components, there is a risk that a single-source supplier could fail to deliver adequate supply, or could suffer a business interruption that could affect our supply of these components.

We obtain some of the components for INOpulse through individual purchase orders executed on an as needed basis

rather than pursuant to long-term supply agreements. Our business, financial condition or results of operations could be adversely affected if any of our principal third-party suppliers or manufacturers experience production problems, lack of capacity or transportation disruptions or otherwise cease producing such components.

We intend to conduct, and may in the future conduct, clinical trials for certain of our product candidates at sites outside the United States, and the FDA may not accept data from trials conducted in such locations.

We have conducted, and may in the future choose to conduct, one or more of our clinical trials outside the United States. For example, our first of two Phase 3 clinical trials of INOpulse for PAH included sites outside of the United States, including Canada.

Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of this data is subject to certain conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with GCP in the case of drug trials, or the Declaration of Helsinki or the laws and regulations of the country in which the research is conducted, whichever affords greater protection to the human subjects, in the case of device trials. The trial population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. Generally, the patient population for any clinical trials conducted outside of the United States must be representative of the population for whom we intend to seek approval in the United States. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will be dependent upon its determination that the trials also complied with all applicable U.S. laws and regulations. There can be no assurance that the FDA will accept data from trials conducted outside of the United States.

In addition, the conduct of clinical trials outside the United States could have a significant impact on us. Risks inherent in conducting international clinical trials include:

- foreign regulatory requirements that could restrict or limit our ability to conduct our clinical trials;
- administrative burdens of conducting clinical trials under multiple foreign regulatory schema;
- foreign exchange fluctuations; and
- diminished protection of intellectual property in some countries.

If clinical trials of our product candidates fail to demonstrate safety and efficacy of our product candidates to the satisfaction of the FDA and comparable non-U.S. regulators, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of these product candidates.

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

Any inability to successfully complete pre-clinical and clinical development could result in additional costs to us and impair our ability to generate revenues from product sales. In addition, if (1) we are required to conduct additional clinical trials or other testing of our product candidates beyond the trials and testing that we contemplate, (2) we are unable to successfully complete clinical trials of our product candidates or other testing, (3) the results of these trials or tests are unfavorable, uncertain or are only modestly favorable, such as in our Phase 2 clinical trials of INOpulse for PAH and INOpulse for PH-COPD, or (4) there are unacceptable safety concerns associated with our product candidates, we, in addition to incurring additional costs, may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as we intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;

- be subject to additional post-marketing testing or other requirements; or
- be required to remove the product from the market after obtaining marketing approval.

If the FDA or other regulatory authority requires us to conduct additional testing or determines that an unacceptable amount of nitrogen dioxide is formed through the use of INOpulse, we may be required to alter the design of INOpulse, which may not be possible, and the clinical development timeline for INOpulse may be delayed or prove to be more costly than we currently anticipate.

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

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

- clinical trials of our product candidates may produce unfavorable or inconclusive results;
- we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, patient enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors, including those manufacturing our product candidates or components or ingredients thereof or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner or at all;
- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching or fail to reach an agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- patients who enroll in a clinical trial may misrepresent their eligibility to do so or may otherwise not comply with the clinical trial protocol, resulting in the need to withdraw such patients from the clinical trial, increase the needed enrollment size for the clinical trial or extend the clinical trial's duration;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their respective standards of conduct, a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate or findings of undesirable effects caused by a chemically or mechanistically similar drug or drug candidate;
- the FDA or comparable non-U.S. regulatory authorities may disagree with our clinical trial design or our interpretation of data from pre-clinical studies and clinical trials;
- the FDA or comparable non-U.S. regulatory authorities may find regulatory non-compliance with the manufacturing processes or facilities of third-party manufacturers with which we enter into agreements for clinical and commercial supplies;
- the supply or quality of raw materials or manufactured product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply; and
- the approval policies or regulations of the FDA or comparable non-U.S. regulatory authorities may significantly change in a manner rendering our clinical data insufficient to obtain marketing approval.

Product development costs for us will increase if we experience delays in testing or pursuing marketing approvals and we may be required to obtain additional funds to complete clinical trials and prepare for possible commercialization of our product candidates. We do not know whether any pre-clinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. For example, although we completed a Phase 2 clinical trial for INOpulse for PH-COPD in 2014, we only began further Phase 2 development in this indication in 2016. Significant pre-clinical study or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations. In addition, many of the factors that cause, or lead to, clinical trial delays may ultimately lead to the denial of marketing approval of any of our product candidates.

If we experience delays or difficulties in the enrollment of patients in clinical trials, we may not achieve our clinical development on our anticipated timeline, or at all, and our receipt of necessary regulatory approvals could be delayed or prevented.

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

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the proximity of patients to clinical sites;
- the eligibility criteria for the trial;
- the design of the clinical trial;
- limitations placed on enrollment by regulatory authorities;
- efforts to facilitate timely enrollment;
- competing clinical trials; and
- clinicians' and patients' perceptions as to the potential advantages and risks of the product candidate being studied in relation to other available therapies, including any new product candidates that may be approved for the indications we are investigating.

For example, we may experience difficulty enrolling our clinical trials, including, but not limited to, any future clinical trials of INOpulse for PH-ILD, or any future clinical trials of INOpulse for PH-COPD because such trials may require that patients meet the restrictive enrollment criteria, such as having been diagnosed with both COPD and PH, be undergoing treatment with LTOT and not having significant left ventricular dysfunction.

Our inability to enroll a sufficient number of patients for our clinical trials could result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, delay or halt the development of and approval processes for our product candidates and jeopardize our ability to achieve our clinical development timeline and goals, including the dates by which we will commence, complete and receive results from clinical trials. Enrollment delays may also delay or jeopardize our ability to commence sales and generate revenues from our product candidates. Any of the foregoing could cause the value of our company to decline and limit our ability to obtain additional financing, if needed.

We may not obtain orphan drug exclusivity for any of our product candidates and indications, or we may not receive the full benefit of orphan drug exclusivity even if we obtain such exclusivity.

Regulatory authorities in some jurisdictions, including the United States and the EU, may designate drugs and biologics intended for the treatment of relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States who have been diagnosed as having the

disease or condition at the time of the submission of the request for orphan drug designation. The FDA has granted orphan drug designation to our nitric oxide program for the treatment of PAH. Accordingly, if we are the first company to receive FDA approval for nitric oxide for the treatment of PAH, we will obtain seven years of marketing exclusivity, during which time the FDA may not approve another product containing nitric oxide as its active ingredient for the treatment of PAH, except under a limited number of situations including a showing that another product is clinically superior. We have not yet applied for orphan drug designation in any jurisdictions outside of the United States.

Even though we have obtained orphan drug designation for our nitric oxide program to treat PAH in the United States, and even if we obtain orphan drug designation for our product candidates in other indications, for our future product candidates or in other jurisdictions, due to the uncertainties associated with developing pharmaceutical products, we may not be the first to obtain marketing approval for any particular orphan indication, or we may not obtain approval for an indication for which we have obtained orphan drug designation. Further, even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not protect the product effectively from competition because different drugs can be approved for the same condition. For example, even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is safer, more effective or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process. Orphan drug exclusivity may be lost if the FDA, or the equivalent regulatory authority in jurisdictions outside of the United States, determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

Serious adverse events, or SAEs, or undesirable side effects or other unexpected properties of our product candidates may be identified during development that could delay or prevent the product candidate's marketing approval.

SAEs or undesirable side effects caused by, or other unexpected properties of, our product candidates could cause us, an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of one or more of our product candidates and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or comparable non-U.S. regulatory authorities. If any of our product candidates is associated with SAEs or undesirable side effects or has properties that are unexpected, we may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many drugs or devices that initially showed promise in clinical or earlier stage testing have later been found to cause undesirable or unexpected side effects that prevented further development of the drug or device.

For example, in our Phase 2 clinical trial for INOpulse for PAH completed in October 2014, SAEs were reported for four patients in the 25 mcg/kg ideal body weight/hour, or mcg, low-dose active treatment arm, including bacteremia, myelodysplastic syndrome, increased shortness of breath, and dyspnea, one of which was assessed as possibly related to trial therapy. In the 75 mcg high-dose active treatment arm, nine patients had SAEs. The most common SAEs reported were syncope and bronchitis/tracheobronchitis, one of which was assessed as possibly related to trial therapy. Discontinuation of trial therapy due to adverse events occurred for two patients in the 75 mcg arm and one subject in the 25 mcg arm. Additional or more SAEs, undesirable side effects or other unexpected properties of INOpulse for PAH or our other product candidates could arise or become known during further clinical development. If such an event occurs during development, clinical trials for our product candidates could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us or our collaborators to cease further development, require us to conduct additional clinical trials or other tests or studies or deny approval of the applicable product candidate. Further, pending discussions with regulatory authorities, we may be required to conduct a drug-drug interaction study of INOpulse for PH-COPD. We expect the FDA to require us primarily to study interactions with long-acting beta agonists, which is the only class of COPD drug that has been identified as having potential adverse cardiac side effects, to confirm that pulsed inhaled nitric oxide does not increase systemic bio-availability of inhaled beta agonists. If the results of such a study indicate increased bioavailability that we are not able to address to the satisfaction of the FDA, marketing approval of INOpulse for PH-COPD, if any, may be limited to patients who do not use long-acting beta agonists.

Additionally, INOpulse is an extension of the technology that is used in hospitals to deliver inhaled nitric oxide to neonates with a form of PH called persistent PH of the newborn. Persistent PH is an FDA-approved use of inhaled nitric oxide, which is currently marketed by Ikaria as INOmax. Because INOpulse draws on the established efficacy and safety of INOmax, if any SAEs or undesirable side effects or other unexpected properties of INOmax or other inhaled nitric oxide delivery systems developed by Ikaria are identified, INOpulse may be adversely affected and we may be required to interrupt, delay or halt our INOpulse clinical trials.

We may not be successful in our efforts to identify or discover additional potential product candidates.

A significant portion of the research that we are conducting involves the development of innovative approaches to the pulsed delivery of nitric oxide. Our drug-device discovery efforts may not be successful in creating drugs or devices that have commercial value or therapeutic utility. Our research programs may initially show promise in creating potential product candidates, yet fail to yield viable product candidates for clinical development for a number of reasons, including that potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be product candidates that will receive marketing approval and achieve market acceptance.

Our research programs to identify new product candidates will require substantial technical, financial and human resources. In addition, we may focus our efforts and resources on one or more potential product candidates that ultimately prove to be unsuccessful.

Pursuant to the terms of our license agreement with Ikaria, we only have the right to develop and commercialize pulsed nitric oxide for the Bellerophon indications; Ikaria retains the right to develop and commercialize inhaled nitric oxide products, including pulsed products, for all other indications. Additionally, we are limited in the scope of potential product candidates that we can identify or discover due to non-competition agreements that we entered into with Ikaria, which agreements were amended in July 2015 and April 2018. In the event that we or one of our subsidiaries materially breach the provisions of the non-competition agreements and do not cure such breach within 30 days after receiving written notice thereof from Ikaria, Ikaria will have the right to terminate the license agreement.

If we are unable to identify suitable additional compounds for pre-clinical and clinical development, or at all, our ability to develop product candidates and obtain product revenues in future periods could be compromised, which could result in significant harm to our financial position and adversely impact our stock price.

If any of our product candidates receives marketing approval and we, or others, later discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, our ability to market the product could be adversely affected.

Clinical trials of our product candidates are conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If, following approval of a product candidate, we, or others, discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following undesirable events could occur:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we may be required to recall the product or change the way the product is administered;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular product;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- we may be required to create a handout, sometimes referred to as a Medication Guide, outlining the risks of the previously unidentified side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Any of these events could have a material and adverse effect on our operations and business and could adversely impact our stock price.

Even if one of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success, and the market opportunity for the product candidate may be smaller than we estimate.

We have never commercialized a product. Even if one of our product candidates is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch therapies due to lack of reimbursement for existing therapies.

Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. If any of our product candidates is approved but does not achieve an adequate level of market acceptance, we may not generate significant revenues and we may not become profitable. The degree of market acceptance of, and potential market opportunity for, our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of the product;
- the potential advantages of the product compared to alternative treatments;
- the prevalence and severity of any side effects;
- the clinical indications for which the product is approved;
- whether the product is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy;
- limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling;
- our ability to offer the product for sale at competitive prices;
- our ability to establish and maintain pricing sufficient to realize a meaningful return on our investment;
- our ability to prevent use of our INOpulse for PH-COPD device by PH-ILD patients due to expected pricing differences;
- the product's convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try, and of physicians to prescribe, the product;
- the strength of sales, marketing and distribution support;
- the approval of other new products for the same indications;
- changes in the standard of care for the targeted indications for the product;
- the timing of market introduction of our approved products as well as competitive products and other therapies;
- availability and amount of reimbursement from government payors, managed care plans, private health coverage insurers and other third-party payors;
- adverse publicity about the product or favorable publicity about competitive products; and
- potential product liability claims.

The potential market opportunities for our product candidates are difficult to estimate precisely. Our estimates of the potential market opportunities, including our estimates with respect to pricing and reimbursement, are predicated on many assumptions, including industry knowledge and publications, third-party research reports and other surveys. While we believe

that our internal assumptions are reasonable, these assumptions involve the exercise of significant judgment on the part of our management, are inherently uncertain and the reasonableness of these assumptions has not been assessed by an independent source. If any of the assumptions proves to be inaccurate, the actual markets for our product candidates could be smaller than our estimates of the potential market opportunities.

If we are unable to establish sales, marketing and distribution capabilities or enter into acceptable sales, marketing and distribution arrangements with third parties, we may not be successful in commercializing any product candidates that we develop, if and when those product candidates are approved.

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. The development of sales, marketing and distribution capabilities will require substantial resources, will be time-consuming and could delay any product launch. We expect that we will commence the development of these capabilities prior to receiving approval of any of our product candidates. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we could have prematurely or unnecessarily incurred these commercialization costs. Such a delay may be costly, and our investment could be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire or retain a sales force in the United States that is sufficient in size or has adequate expertise in the medical markets that we plan to target. If we are unable to establish or retain a sales force and marketing and distribution capabilities, our operating results may be adversely affected.

If a potential partner has development or commercialization expertise or financial resources that we believe is particularly relevant to one of our product candidates, then we may seek to collaborate with that potential partner even if we believe we could otherwise develop and commercialize the product independently. We may partner with third parties to commercialize our product candidates in certain countries outside the United States. As a result of entering into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues may be lower, perhaps substantially lower, than if we were to directly market and sell products in those markets. Furthermore, we may be unsuccessful in entering into the necessary arrangements with third parties or may be unable to do so on terms that are favorable to us. In addition, we may have little or no control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our product candidates effectively.

If we do not establish sales and marketing capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing any of our product candidates that receive marketing approval.

Even if we are able to commercialize any product candidate that we develop, the product may become subject to unfavorable pricing regulations, third-party payor reimbursement practices or healthcare reform initiatives that could harm our business.

The commercial success of our product candidates will depend substantially, both in the United States and abroad, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish and maintain pricing sufficient to realize a meaningful return on our investment.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved drugs and devices. Marketing approvals, pricing and reimbursement for new drug and device products vary widely from country to country. Some countries require approval of the sale price of a drug or device before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some non-U.S. markets, pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our ability to commercialize our product candidates will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability to sell our product candidates profitably. These payors may not view our products, if any, as cost-effective, and coverage and reimbursement may not be available to our customers, or may not be sufficient to allow our products, if any, to be marketed on a competitive basis. Cost-control initiatives could cause us to decrease the price we might establish for products, which could result in lower than anticipated product revenues. If the prices for our products, if any, decrease or if governmental and other third-party payors do not provide adequate coverage or reimbursement, our prospects for revenue and profitability will suffer. Approval of a product does not guarantee sufficient reimbursement to achieve commercial success.

There may also be delays in obtaining coverage and reimbursement for newly approved products, and coverage may be more limited than the indications for which the product is approved by the FDA or comparable non-U.S. regulatory authorities. Moreover, eligibility for reimbursement does not imply that any product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Reimbursement rates may vary, by way of example, according to the use of the product and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost products or may be incorporated into existing payments for other services.

In addition, increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. We cannot be sure that coverage will be available for any product candidate that we commercialize and, if available, that the reimbursement rates will be adequate. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any our product candidates for which we obtain marketing approval could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

If the FDA or comparable non-U.S. regulatory authorities approve generic versions of any of our products that receive marketing approval, or such authorities do not grant our products appropriate periods of data exclusivity before approving generic versions of our products, the sales of our products could be adversely affected.

Once an NDA is approved, the product covered thereby becomes a “reference listed drug” in the FDA’s publication, “Approved Drug Products with Therapeutic Equivalence Evaluations.” Manufacturers may seek approval of generic versions of reference listed drugs through submission of ANDAs in the United States, or through a similar process in foreign jurisdictions. In support of an ANDA, a generic manufacturer need not conduct clinical studies. Rather, the applicant generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labeling as the reference listed drug and that the generic version is bioequivalent to the reference listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference listed drug and companies that produce generic products are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference listed drug may be typically lost to the generic product.

The FDA may not approve an ANDA for a generic product until any applicable period of non-patent exclusivity for the reference listed drug has expired. Manufacturers may seek to launch these generic products following the expiration of the applicable marketing exclusivity period, even if we still have patent protection for our product.

Competition that our products may face from generic versions of our products could materially and adversely impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made in those product candidates.

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

We face an inherent risk of product liability claims as a result of the clinical testing of our product candidates despite obtaining appropriate informed consents from our clinical trial participants. We will face an even greater risk if we

commercially sell any product that we may develop. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. For example:

- improper use or failure of INOpulse may result in rebound PH, which can be fatal in some patients;
- rebound PH may also occur if both the primary and back-up devices fail before we can replace them, if the built-in back-up with a device does not work properly or if the patient does not carry or have access to his or her back-up device; and
- rebound PH can also occur in patients who were not previously considered at risk for this reaction and who may not have been provided an adequate back-up device.
- Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Regardless of the merits or eventual outcome, liability claims may result in:
    - decreased demand for products that we may develop;
    - injury to our reputation and significant negative media attention;
    - withdrawal of clinical trial participants;
    - significant costs to defend resulting litigation;
    - substantial monetary awards to trial participants or patients;
    - loss of revenue;
    - reduced resources of our management to pursue our business strategy; and
    - the inability to commercialize any products that we may develop.

Although we maintain general liability insurance of $1.0 million in the aggregate, umbrella insurance in the amount of $10.0 million in the aggregate and clinical trial liability insurance of $20.0 million in the aggregate, this insurance may not fully cover potential liabilities that we may incur. The cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial. We will need to increase our insurance coverage if and when we begin the commercial sale of any product candidate that receives marketing approval. In addition, insurance coverage is becoming increasingly expensive. If we are unable to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of our product candidates, which could adversely affect our business, financial condition, results of operations and prospects.

Our INOpulse devices use lithium-ion battery cells, which have been observed to catch fire or vent smoke and flame, and these events may raise concerns about the batteries we use.

The battery pack used in our INOpulse devices makes use of lithium-ion cells. On rare occasions, lithium-ion cells can rapidly release the energy they contain by venting smoke and flames in a manner that can ignite nearby materials. Highly publicized incidents of laptop computers and cell phones bursting into flames have focused consumer attention on the safety of these cells. There can be no assurance that the battery packs we use would not fail, which could lead to property damage, personal injury or death, and may subject us to lawsuits. We may also have to recall our products, if any, which would be time consuming and expensive. Also, negative perceptions in the healthcare and patient communities regarding the suitability of lithium-ion cells for medical applications or any future incident involving lithium-ion cells could seriously harm our business, even in the absence of an incident involving us.

Risks Related to Our Dependence on Third Parties

The intellectual property underlying INOpulse is exclusively licensed from Ikaria. If Ikaria terminates the license agreement, or fails to prosecute, maintain or enforce the underlying patents, our business will be materially harmed.

We have licensed the intellectual property underlying INOpulse from Ikaria. The license agreement prohibits us from sublicensing to any competitor of Ikaria any intellectual property licensed to us by Ikaria. In addition, we are required to ensure that all of our products candidates are used solely for the chronic treatment of the Bellerophon indications and to enter into written agreements with any customers that contain restrictions on the use of our products and termination rights in the event such restrictions are violated.

Ikaria has the initial right, but not the obligation, to prosecute and maintain all patents that are licensed to us pursuant to the license agreement. While we have certain step-in rights to assume control if Ikaria declines to file, prosecute or maintain certain licensed patents that are core to our business, in the event Ikaria reasonably determines that our actions could materially impair its business operations or intellectual property rights, Ikaria may prohibit us from taking such actions. In addition, Ikaria has the initial right, but not the obligation, to initiate a legal action against a third party with respect to any actual or suspected infringement of patent rights licensed to us pursuant to the license agreement. We have the right to initiate legal action against a third-party infringer of licensed patents that are core to our business in the event Ikaria declines to take action with respect to such infringement, however, if Ikaria determines that our pursuit of any such action could materially impair its business operations or intellectual property rights, Ikaria may prohibit us from taking any such action.

The license agreement terminates, on an INOpulse product-by-INOpulse product basis, at such time as we are no longer actively and continuously engaged in the development or commercialization of such product. In addition, Ikaria may terminate the license agreement if, among other things, (1) we breach or fail to comply with any material term or condition required to be performed or complied with by us and do not cure such breach or failure within 30 days after receiving written notice of such breach from Ikaria, (2) we or any of our affiliates breaches any of our agreements not to compete with Ikaria, (3) we or any of our affiliates challenges the validity or enforceability of the licensed patents or (4) we or any person that is a successor to our license rights markets a generic nitric oxide product that is competitive with Ikaria's INOmax product. Upon termination of the license agreement with respect to any INOpulse product candidate, we will lose our ability to market such INOpulse product candidate, and upon Ikaria's written request, be required to transfer any and all regulatory approvals relating to such INOpulse product candidate to Ikaria.

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

We currently rely on third-party companies to conduct our clinical trials. We expect to continue to rely on third parties, such as clinical research organizations, or CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials. Our agreements with these third parties generally allow the third party to terminate the agreement at any time. If we are required to enter into alternative arrangements because of any such termination, the introduction of our product candidates to market could be delayed.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we design our clinical trials and will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with GCPs for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified time frames. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

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

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.

We have entered into a drug clinical supply agreement with Ikaria, pursuant to which Ikaria will manufacture and supply our requirements for nitric oxide for inhalation and corresponding placebo for use in clinical trials of INOpulse. Ikaria manufactures pharmaceutical-grade nitric oxide at its facility in Port Allen, Louisiana, which is the only FDA-inspected site in the world for manufacturing medical nitric oxide. Ikaria's Port Allen facility is subject to the risks of a natural disaster or other business disruption. We maintain under controlled storage conditions a two- to three-month supply of clinical trial drug product, but there can be no assurance that we would be able to meet our requirements for INOpulse if there were a catastrophic event or failure of Ikaria's manufacturing system. Because Ikaria's Port Allen facility is the only FDA-inspected site that can manufacture nitric oxide for INOpulse and because the manufacture of a pharmaceutical gas requires specialized equipment and expertise, there are few, if any, third-party manufacturers to which we could contract this work in a short period of time. Therefore, any disruption in Ikaria's Port Allen facility, or the failure by Ikaria for any other reason to provide us with nitric oxide, could materially and adversely affect supplies of nitric oxide for INOpulse and our ongoing and planned clinical trials. Any such disruption would force us to seek nitric oxide from an alternative source, which may not be available on commercially reasonable terms, or at all. In addition, we do not currently have any arrangements with Ikaria to provide us with commercial quantities of nitric oxide. If we are unable to arrange for Ikaria to provide such quantities on commercially reasonable terms, or at all, we may not be able to successfully produce and market INOpulse or may be delayed in doing so.

We rely on third-party suppliers and manufacturers to produce and deliver clinical devices and supplies as well as for the servicing of these devices for our INOpulse product candidates, and may also do so for other product candidates. Any failure by a third-party supplier or manufacturer to produce or deliver supplies for us or to provide necessary servicing may delay or impair our ability to complete our clinical trials or commercialize our product candidates.

We currently rely, and expect to continue to rely, on third parties for supply of the device, cannula and certain other supplies for our INOpulse product candidates. These suppliers are, and any future third-party suppliers with whom we enter into agreements may be, our sole suppliers of these devices or any of our other current or future devices used in the INOpulse program. These suppliers are commonly referred to as single-source suppliers. If our suppliers fail to deliver materials and provide services needed for the production of the INOpulse device and related supplies or for our other product candidates in a timely and sufficient manner, if they fail to comply with applicable regulations, or if we do not qualify alternate suppliers, clinical development or regulatory approval of our product candidates or commercialization of our products could be delayed, increasing our costs to complete clinical development and to obtain regulatory approval, which could deprive us of potential additional product revenue.

If one or more of our product candidates are approved by the FDA or comparable regulatory authorities in other countries for commercial sale, we will need to manufacture such product candidate in larger quantities. We do not currently have any arrangements with Ikaria or any other third-party manufacturer to provide commercial quantities of our product candidates. If we are unable to arrange for such a third-party manufacturing source, or fail to do so on commercially reasonable terms, we may not be able to successfully produce and market our product candidates or may be delayed in doing so.

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 have exclusively licensed INOpulse, for certain indications and settings, and subject to certain retained rights of the licensor, from Ikaria. We may also enter into additional license agreements as part of the development of our business in the future. Such licensors, if any, may be responsible for prosecution of certain patent applications and maintenance of certain patents. Such licensors may not successfully prosecute such patent applications or maintain such patents, which we have licensed and on which our business depends. Our licensors may fail to pursue litigation against third-party infringers, may fail to prove infringement, or may fail to defend against counterclaims of patent invalidity or unenforceability. If these in-licenses are terminated, or if the underlying patents fail to provide the intended market exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products identical to ours. This could have a material adverse effect on our competitive business position and our business prospects.

Third parties may seek to hold us responsible for liabilities of Ikaria that we did not assume in our agreements.

In connection with our separation from Ikaria, Ikaria has generally agreed to retain all liabilities that did not historically arise from our business. Third parties may seek to hold us responsible for Ikaria's retained liabilities. Under our agreements

with Ikaria, Ikaria has agreed to indemnify us for claims and losses relating to these retained liabilities. However, if those liabilities are significant and we are ultimately liable for them, we cannot assure our stockholders that we will be able to recover the full amount of our losses from Ikaria.

Any disputes that arise between us and Ikaria with respect to our past and ongoing relationships could harm our business operations.

Disputes may arise between Ikaria and us in a number of areas relating to our past and ongoing relationships, including:

- intellectual property, technology and business matters, including failure to make required technology transfers and failure to comply with non-compete provisions applicable to Ikaria and us;
- labor, tax, employee benefit, indemnification and other matters arising from our separation from Ikaria;
- distribution and supply obligations;
- employee retention and recruiting;
- business combinations involving us;
- the nature, quality and pricing of transitional services Ikaria has agreed to provide us; and
- business opportunities that may be attractive to both Ikaria and us.

We may not be able to resolve any potential conflicts, and even if we do, the resolution may be less favorable than if we were dealing with an unaffiliated party.

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.

We may seek third-party collaborators for development and commercialization of our product candidates. Our likely collaborators for any marketing, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical and medical device companies, regional and national biotechnology companies and pharmaceutical companies. We are not currently party to any such arrangement. However, if we do enter into any such arrangements with any third parties in the future, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates would pose certain risks to us, including:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators with marketing and distribution rights to one or more of our products may not commit sufficient

resources to the marketing and distribution of such product or products;

- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our products or product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

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

If we are not able to establish collaborations, we may have to alter our development and commercialization plans.

Our drug and device development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with biotechnology and pharmaceutical companies for the development and potential commercialization of those product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. The terms of our current or future license agreements may restrict our ability to enter into agreements on certain terms with future collaborators. For example, our license agreement with Ikaria prohibits us from granting a sublicense under any of the intellectual property licensed to us under such license agreement to any of our affiliates or any third party, in each case, which directly or indirectly competes with the Ikaria nitric oxide business, and any future license agreements may contain similar restrictions. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

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

Risks Related to Our Intellectual Property

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.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology and products. We seek to protect our proprietary position by filing patent

applications in the United States and abroad related to our technologies and product candidates. The patents we have licensed from Ikaria relating to INOpulse's feature of providing delivery of nitric oxide to ensure a consistent dose over time expire as late as 2027 in the United States and as late as 2026 in certain other countries, as well as a patent with respect to the triple-lumen cannula that allows for safer and more accurate dosing of pulsed inhaled nitric oxide, which expires in 2033.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, pursuant to our license agreement with Ikaria, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering the INOpulse technology that we license from Ikaria, except in the event that Ikaria declines to prosecute or maintain certain licensed patents that are core to our business, elects to allow any of such patents to lapse or elects to abandon any such patents, in which case we would have step-in rights to assume control of the prosecution and/or maintenance of such patents, subject to Ikaria's right to prohibit us from taking such actions if it reasonably determines that such actions could materially impair its business, operations or intellectual property rights. Similarly, under the terms of any future agreements that we may enter into with other third parties, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering the technology that is licensed to us under such agreements. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of non-U.S. countries may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than U.S. law does. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, and in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not issue as patents that protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our owned or licensed issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. The Leahy-Smith Act includes provisions that affect the way patent applications are prosecuted and affect patent litigation. The USPTO recently developed new regulations and procedures to govern administration of the Leahy-Smith Act. Many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned or licensed patent applications and the enforcement or defense of our owned or licensed issued patents, all of which could have a material adverse effect on our business and financial condition.

Moreover, we may be subject to third-party preissuance submissions of prior art to the USPTO, or become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging our owned or licensed patent rights or the patent rights of others. For example, Notices of Opposition to two European patents covering BCM that we licensed from BioLine have been filed with the European Patent Office. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Even if our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us, or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. We may not receive patent term extension under the Hatch-Waxman Act that we expect or our rights during the extension period may be more limited than the full scope of the patent, making it easier

for our competitors to develop and market non-infringing technologies or products.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate, or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

Competitors may infringe our owned or licensed patents or other intellectual property. To counter infringement or unauthorized use, we may be required to file or participate in infringement claims, which can be expensive and time consuming. Any claims we or our licensors assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours or our licensor is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our owned or licensed patents at risk of being invalidated or interpreted narrowly.

Under the terms of our license agreement with Ikaria, in the event a third party is suspected of infringing any patent rights licensed to us by Ikaria, Ikaria has the initial right, but not the obligation, to initiate a legal action against such third party. In the event that Ikaria declines to take any action with respect to an alleged infringement of certain licensed patents that are core to our business, we have the right, in certain circumstances, to initiate a legal action against such third party, provided that, if Ikaria reasonably determines that our pursuit of any action with respect to infringement of any of such core patents could materially impair Ikaria's business operations or intellectual property rights, Ikaria may require us to not undertake or to cease any such action. Our inability to initiate a legal action against a third party suspected of infringing intellectual property rights important to our business may have a material adverse effect on our competitive business position and our business prospects.

If we fail to comply with our obligations under license agreements, we could lose rights that are important to our business.

Under our license agreement with Ikaria, we have granted Ikaria a sole and exclusive worldwide license to any intellectual property rights that we control for use in Ikaria's nitric oxide business, and we are required to ensure that all of our products, if any, are used solely for the chronic treatment of Bellerophon indications and to enter into written agreements with any customers that contain restrictions on the use of our products and termination rights in the event such restrictions are violated. We have also agreed to pay 100% of the reasonable and documented costs incurred by Ikaria for the prosecution and maintenance of certain licensed patents that are core to our business and 10% of such costs incurred by Ikaria for all other licensed patents. If we fail to comply with our obligations under current or future license agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product that is covered by the agreement or face other penalties under the agreement. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the pharmaceutical, biotechnology and medical device industries. We may become party to, or be threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference or derivation proceedings before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future.

If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to

cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

We may be subject to claims by third parties asserting that we or our employees have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at other pharmaceutical, biotechnology or medical device companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

In addition, while it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in timely obtaining such an agreement with each party who in fact develops intellectual property that we regard as our own. Even if timely obtained, such agreements may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we fail in prosecuting or defending any such claims, we may lose valuable intellectual property rights or personnel, in addition to paying monetary damages. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

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

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. Even if we are successful in prosecuting such claims, any remedy awarded may be insufficient to fully compensate us for the improper disclosure or misappropriation. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

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

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

- Others may be able to develop and commercialize treatments that are similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed.
- We or our licensors might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed.
- We or our licensors might not have been the first to file patent applications covering certain of our inventions.
- Others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights.
- It is possible that our pending patent applications will not lead to issued patents.
- Issued patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors.
- Our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets.
- We may not develop additional proprietary technologies that are patentable.
- The patents of others may have an adverse effect on our business.
- Another party may be granted orphan drug exclusivity for an indication that we are seeking before us or may be granted orphan drug exclusivity for one of our products for another indication.

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

Even if we complete the necessary clinical trials, the marketing approval process is expensive, time consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA and similar regulatory authorities outside the United States. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. Our product candidates are in the early stages of development and are subject to the risks of failure inherent in drug and device development. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. We have only limited experience in conducting and managing the clinical trials, and in filing and supporting the applications necessary to gain marketing approvals and may rely on third-party CROs to assist us in this process. Securing marketing approval requires the submission of extensive pre-clinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are

insufficient for approval and require additional pre-clinical, clinical or other studies. In addition, varying interpretations of the data obtained from pre-clinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable. If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

Our failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed abroad, and any approval we are granted for our product candidates in the United States would not assure approval of product candidates in foreign jurisdictions.

In order to market and sell our products in the EU and many other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

Even if we obtain marketing approval for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we manufacture and market our products and compliance with such requirements may involve substantial resources, which could materially impair our ability to generate revenue.

Even if marketing approval of a product candidate is granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation, including the requirement to implement a risk evaluation and mitigation strategy or to conduct costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. We must also comply with requirements concerning advertising and promotion for any of our product candidates for which we obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we will not be able to promote any products we develop for indications or uses for which they are not approved. In addition, manufacturers of approved products and those manufacturers' facilities are required to ensure that quality control and manufacturing procedures conform to cGMP, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We and our contract manufacturers could be subject to periodic unannounced inspections by the FDA and other regulatory authorities to monitor and ensure compliance with cGMP.

Accordingly, assuming we receive marketing approval for one or more of our product candidates, we and our contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we are not able to comply with post-approval regulatory requirements, we could have the marketing approvals for our products withdrawn by regulatory authorities and our ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Thus, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Any product candidate for which we obtain marketing approval will be subject to strict enforcement of post-marketing requirements and we could be subject to substantial penalties, including withdrawal of our product from the market, if we fail to comply with all regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include, but are not limited to, restrictions governing promotion of an approved product, submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping.

The FDA and other federal and state agencies, including the Department of Justice, closely regulate compliance with all requirements governing prescription drug and device products, including requirements pertaining to marketing and promotion of drugs and devices in accordance with the provisions of the approved labeling and manufacturing of products in accordance with cGMP requirements. Violations of such requirements may lead to investigations alleging violations of the Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act and other federal and state health care fraud and abuse laws as well as state consumer protection laws. Our failure to comply with all regulatory requirements, and later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, may yield various results, including:

- litigation involving patients taking our products;
- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- untitled or warning letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Non-compliance by us or any future collaborator with regulatory requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with regulatory requirements regarding the protection of personal information could also lead to significant penalties and sanctions.

We will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations after we obtain FDA approval and begin to commercialize our products, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

After we obtain marketing approval, we will be subject to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. Restrictions under applicable 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, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service,

for which payment may be made under a federal healthcare program such as Medicare and Medicaid;

- the federal False Claims Act imposes criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented false or fraudulent claims for payment by a federal government program, or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and 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 ACA, requires applicable manufacturers of covered drugs, devices, biologics 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 laws and regulations such as state anti-kickback and false claims laws and analogous non-U.S. fraud and abuse laws and regulations, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and 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. 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 and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and non-U.S. laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain product candidates and products outside of the United States and require us to develop and implement costly compliance programs.

If we expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act, or the FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of such third party in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the company, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

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

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing or selling certain product candidates and products outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

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

Currently, we do not operate any research and development or production facilities, including laboratory, development or manufacturing facilities. However, if we decided to operate our own research and development and production facilities, we would be subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Such operations may involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and wastes, we would not be able to eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use or disposal of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we would increase our level of workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not expect to maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our possible future storage or disposal of biological, hazardous or radioactive materials.

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

Changes in law or policy could have a negative impact on the approval of our drug candidates.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. Notably, on January 23, 2017, President Trump ordered a hiring freeze for all executive departments and agencies, including the FDA, which prohibits the FDA from filling employee vacancies or creating new positions. Under the terms of the order, the freeze will remain in effect until implementation of a plan to be recommended by the Director for the Office of Management and Budget, or OMB, in consultation with the Director of the Office of Personnel Management, to reduce the size of the federal workforce through attrition. An under-staffed FDA could result in delays in FDA's responsiveness or in its ability to review submissions or applications, issue regulations or guidance, or implement or enforce regulatory requirements in a timely fashion or at all. Moreover, on January 30, 2017, President Trump issued an Executive Order, applicable to all executive agencies, including the FDA, which requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This Executive Order includes a budget neutrality provision that requires the total incremental cost of

all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the Executive Order requires agencies to identify regulations to offset any incremental cost of a new regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within OMB on February 2, 2017, the administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. It is difficult to predict how these requirement will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

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

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

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

Risks Related to Employee Matters and Managing Growth

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

We are dependent on the scientific, business development and clinical expertise of our management team. Leadership transitions can be inherently difficult to manage and may cause some disruptions in our business.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. Any of our employees may terminate their employment with us at any time. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. We do not maintain "key person" insurance for any of our executives or other employees. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical, biotechnology and medical device companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations, to provide accurate information to the FDA, to comply with federal and state healthcare fraud and abuse laws and regulations, to report financial information or data accurately, to disclose unauthorized activities to us or to comply with our code of business conduct and ethics. In particular, sales, marketing and business

arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, false claims, inappropriate promotion, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. The precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

In addition, during the course of our operations, our directors, executives and employees may have access to material, non-public information regarding our business, our results of operations or potential transactions we are considering. We may not be able to prevent a director, executive or employee from violating our insider trading policies and trading in our common stock on the basis of, or while having access to, material, non-public information. If a director, executive or employee was to be investigated, or an action was to be brought against a director, executive or employee for insider trading, it could have a negative impact on our reputation and our stock price. Such a claim, with or without merit, could also result in substantial expenditures of time and money, and divert attention of our management team from other tasks important to the success of our business.

Risks Related to Ownership of Our Common Stock

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

Our executive officers, directors and stockholders who are known by us to beneficially own more than 5% of our common stock, in the aggregate, beneficially owned a majority of our outstanding common stock as of March 12, 2019. As a result, if these stockholders were to choose to act together, they would be able to exert a significant degree of influence over matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, could delay, defer or prevent a change in control; entrench our management or board of directors; or impede a merger, consolidation, takeover or other business combination involving us that other stockholders may desire.

In addition, as of March 12, 2019, our largest stockholder, investment funds affiliated with New Mountain Capital, or the New Mountain Entities, beneficially owned, in the aggregate, approximately 22% of our outstanding common stock. Pursuant to the terms of a stockholders agreement, the New Mountain Entities are 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 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 aggregate number 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 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).

The New Mountain Entities also have certain other rights conferred by the stockholders agreement. The New Mountain Entities may exert significant influence over matters requiring board approval. In addition, their consent is required for certain matters requiring approval by our stockholders, including the compensation and hiring and firing of our chief executive officer, business combinations, issuance of shares of our capital stock and incurrence of debt. These stockholder approval rights will terminate as outlined in the section entitled “Certain Relationships and Related Person Transactions-Stockholders Agreements” in our 2019 Proxy Statement (as defined below in Part III).

Our second largest stockholder, Puissance, beneficially owned approximately 12% of our outstanding common stock as of March 12, 2019.

Our third largest stockholder, Venrock Healthcare, beneficially owned approximately 10.7% of our outstanding common stock as of March 12, 2019.

Our fourth largest stockholder, Linde North America, Inc., an indirect wholly-owned subsidiary of Linde AG, or Linde, beneficially owned approximately 7.7% of our outstanding common stock, as of March 12, 2019. Pursuant to the terms of a stockholders agreement, Linde is entitled to designate one director to our board of directors and to designate one director to the board of directors (or equivalent governing body) of each of our subsidiaries if continuing ownership requirements are met as

outlined in the section entitled “Certain Relationships and Related Person Transactions-Stockholders Agreements” in our 2019 Proxy Statement (as defined below in Part III).

The New Mountain Entities, Puissance, Venrock and Linde may have interests that differ from the interests of our other stockholders, and they may vote in ways with which our other stockholders disagree and that may be adverse to interests of our other stockholders. The concentration of ownership of our capital stock may have the effect of delaying, preventing or deterring a change of control of our company, could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company and may adversely affect the market price of our common stock.

A significant portion of our total outstanding shares are subject to volume limitations as to sale, but have registration rights that could allow them to be sold into the market without such restrictions, which could cause the market price of our common stock to drop significantly, even if our business is performing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time, subject to certain restrictions described below. These sales, or the perception in the market that holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Certain holders of a significant number of shares of our common stock have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. Many of these shares could be freely sold without registration subject to the volume limitations applicable to affiliates under Rule 144. As of March 12, 2019, we had outstanding options to purchase an aggregate of 7,040,044 shares of our common stock, of which options to, purchase approximately 2,390,807 were vested and outstanding and outstanding warrants to purchase an aggregate of 34,251,014 shares of our common stock. These shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price or trading volume of our stock could decline.

The trading market for our common stock relies, in part, on the research and reports that industry or financial analysts publish about us or our business. If no, or few, analysts commence coverage of us, the trading price of our stock would likely decrease. Even if we do obtain analyst coverage, if one or more of the analysts covering our business do not publish favorable reports or downgrade their evaluations of our stock, the price of our stock could decline. If one or more analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price or trading volume to decline.

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

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

- actual or anticipated results from and any delays in our clinical trials, including our expected and ongoing clinical trials of our INOpulse product candidates, as well as results of regulatory input on our clinical trial programs and regulatory reviews relating to the approval of our product candidates;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- failure or discontinuation of any of our clinical development programs;
- the level of expenses related to any of our product candidates or clinical development programs;
- commencement or termination of any collaboration or licensing arrangement;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures and capital commitments;

- additions or departures of key scientific or management personnel;
- variations in our financial results or those of companies that are perceived to be similar to us;
- new products, product candidates or new uses for existing products introduced or announced by our competitors, and the timing of these introductions or announcements;
- results of clinical trials of product candidates of our competitors;
- general economic and market conditions and other factors that may be unrelated to our operating performance or the operating performance of our competitors, including changes in market valuations of similar companies;
- regulatory or legal developments in the United States and other countries;
- changes in the structure of healthcare payment systems;
- conditions or trends in the pharmaceutical, biotechnology and medical device industries;
- actual or anticipated changes in earnings estimates, development time lines or recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- sales of common stock by us or our stockholders in the future, as well as the overall trading volume of our common stock; and
- the other factors described in this “Risk Factors” section.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

In the past, following periods of volatility in the market price of a company’s securities, securities class-action litigation often has been instituted against that company. Such litigation, if instituted against us, could cause us to incur substantial costs to defend such claims and divert management’s attention and resources, which could seriously harm our business, financial condition, results of operations and prospects.

An active trading market for our common stock may not be sustained.

Our shares of common stock began trading on the Nasdaq Global Market on February 13, 2015. Given the limited trading history of our common stock, there is a risk that an active trading market for our shares may not continue to develop or be sustained. If an active market for our common stock does not continue to develop or is not sustained, it may be difficult for investors to sell shares without depressing the market price for the shares, or at all.

If we are unable to meet the continued listing requirements of the Nasdaq Global Market and Nasdaq determines to delist our common stock, the market liquidity and market price of our common stock could decline.

Our common stock is listed on the Nasdaq Global Market. On February 27, 2019, we received a notification letter from The Nasdaq Stock Market ("Nasdaq") indicating that our common stock no longer meets the minimum bid price requirement for continued listing on the Nasdaq Global Market as set forth in Listing Rule 5450(a)(1). The letter gave us notice that the bid price of our common stock has closed under $1.00 for the last 30 consecutive business days. The notification did not result in the immediate delisting of our common stock from the Nasdaq Global Market. We have until August 26, 2019 to regain compliance with the minimum closing bid price requirement. To regain compliance, the closing bid price of our common stock must meet or exceed $1.00 per share for at least ten consecutive business days. If we do not regain compliance by August 26, 2019, we may submit a transfer application to the Nasdaq Capital Market in order to receive an additional 180-day compliance period to comply. In order to be eligible for the transfer and additional time, we will be required to meet the continued listing requirement for market value of publicly held shares and all of the initial listing requirements for the Nasdaq Capital Market,

other than the minimum bid price requirement, and must notify Nasdaq in writing of our intention to cure the deficiency during the second compliance period. We are considering actions that we may take in response to this notification in order to regain compliance with the continued listing requirements. A delisting of our common stock from Nasdaq could materially reduce the liquidity of our common stock and result in a corresponding material reduction in the price of our common stock. In addition, delisting could harm our ability to raise capital through alternative financing sources on terms acceptable to us, or at all, and may result in the potential loss of confidence by investors, employees and fewer business development opportunities.

We have broad discretion in the use of our cash and cash equivalents and may not use them effectively.

Our management has broad discretion in the application of our cash and cash equivalents and could spend these funds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest our cash and cash equivalents in a manner that does not produce income or that loses value.

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

We are an "emerging growth company," as defined in the 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 $1.07 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 the last business day of our most recently completed second fiscal quarter. 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 our filings with the SEC. 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.

We are currently incurring and expect to continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

We completed our IPO in February 2015. As a public company, we incur and expect to continue to incur significant legal, accounting and other expenses. We expect that our expenses will further increase after we are no longer an "emerging growth company." We expect that we will need to hire additional accounting, finance and other personnel to comply with the requirements of being a public company, and our management and other personnel will need to devote a substantial amount of

time towards maintaining compliance with these requirements. In addition, the Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the SEC and Nasdaq have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. Many of the internal controls over financial reporting have not been tested. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed time frame that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Our certificate of incorporation provides that the doctrine of "corporate opportunity" will not apply to any of our stockholders or directors, except in limited circumstances, which may adversely affect our business or prospects.

Our certificate of incorporation provides that the doctrine of "corporate opportunity" will not apply to any of our stockholders or directors, other than any stockholder or director that is an employee of ours. The doctrine of corporate opportunity generally provides that a corporate fiduciary may not develop an opportunity using corporate resources, acquire an interest adverse to that of the corporation or acquire property that is reasonably incident to the present or prospective business of the corporation or in which the corporation has a present or expectancy interest, unless that opportunity is first presented to the corporation and the corporation chooses not to pursue that opportunity. The doctrine of corporate opportunity is intended to preclude officers or directors from personally benefiting from opportunities that belong to the corporation. We have renounced any prospective corporate opportunity so that our stockholders and directors (other than those that are employees of ours) and their respective representatives have no duty to communicate or present corporate opportunities to us, including any opportunity that becomes known to Ikaria and its directors, 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, including to Ikaria. 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. Therefore, we may be in competition with our stockholders, directors or their respective affiliates, and we may not have knowledge of, or be able to pursue, a transaction that could potentially be beneficial to us. Accordingly, we may lose a corporate opportunity or suffer competitive harm, which could negatively impact our business or prospects.

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

Our certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our certificate of incorporation or our bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine. This provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. Alternatively, if a court were to find this provision in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

Provisions in our certificate of incorporation, our bylaws or Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the trading price of our common stock.

Provisions of our certificate of incorporation, our bylaws or Delaware law may discourage, delay or prevent a merger, acquisition or other change in control that stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions may also prevent or frustrate attempts by our stockholders to change the composition of our board of directors or to replace or remove our management. These provisions include:

- limitations on the removal of directors;
- a classified board of directors so that not all members of our board are elected at one time;
- advance notice requirements for stockholder proposals and nominations;
- limitations on the ability of stockholders to call and bring business before special meetings and to take action by written consent in lieu of a meeting;
- limitations on the liability of, and the provision of indemnification to, our director and officers; and
- the ability of our board of directors to authorize the issuance of blank check preferred stock, which could be issued with voting, liquidation, dividend and other rights superior to our common stock.

In addition, we are subject to Section 203 of the Delaware General Corporation Law, which prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

The existence of the foregoing provisions and anti-takeover measures could limit the price that investors might be willing to pay in the future for shares of our common stock. They could also deter potential acquirers of our company, thereby reducing the likelihood that investors could receive a premium for their shares of our common stock in an acquisition.

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

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our principal facilities consist of approximately 22,000 square feet of office space at our headquarters located in Warren, New Jersey and approximately 1,600 square feet of office space and research lab facilities at the Commercialization Center for Innovative Technologies located in North Brunswick, New Jersey. We lease the space in Warren, New Jersey under a lease that expires in 2023. We lease the space in North Brunswick, New Jersey under a month-to-month lease. We believe that we have adequate space for our anticipated needs and that suitable additional space will be available at commercially reasonably terms as needed.

Item 3. Legal Proceedings

We are not presently a party to any material litigation or regulatory proceeding, and we are not aware of any pending or threatened litigation or regulatory proceeding against us that could have a material adverse effect on our business, operating results, financial condition or cash flows.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

Market Information

The Company's Common Stock is traded on The Nasdaq Stock Market under the symbol "BLPH".

Stockholders

As of March 12, 2019, there were approximately 230 holders of record of our common stock. This number does not include beneficial owners whose shares are held by nominees in street name.

Recent Sales of Unregistered Securities

None.

Issuer Purchases of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

Item 6. Selected Financial Data

The following selected financial data should be read together with our financial statements and the related notes appearing elsewhere in this Annual Report on Form 10-K and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this Annual Report on Form 10-K. We have derived the statements of operations data for the years ended December 31, 2018, 2017 and 2016 and the balance sheet data as of December 31, 2018 and 2017 from our audited financial statements included elsewhere in this Annual Report on Form 10-K, which have been audited by KPMG LLP, an independent registered public accounting firm. The balance sheet data as of December 31, 2016, 2015 and 2014 as well as the Statement of Operations data for the years ended December 31, 2015 and 2014 are from our audited financial statements that are not included in this Annual Report on Form 10-K. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period.

(in thousands, except per share/unit data)	Year Ended December 31, 2018	2017	2016	2015	2014
Consolidated Statement of Operations Information					
Operating expenses:					
Research and development	$ 20,259	$ 17,854	$ 16,650	$ 33,365	$ 45,978
General and administrative	7,621	6,745	7,107	14,870	13,775
Total operating expenses	27,880	24,599	23,757	48,235	59,753
Other operating income	—	—	—	1,667	—
Loss from operations	(27,880)	(24,599)	(23,757)	(46,568)	(59,753)
Change in fair value of common stock warrant liability	24,877	(30,403)	(590)	—	—
Interest and other income, net	378	184	95	109	79
Pre-tax loss	(2,625)	(54,818)	(24,252)	(46,459)	(59,674)
Income tax benefit	(5,439)	—	(438)	—	—
Net income (loss)	$ 2,814	$ (54,818)	$ (23,814)	$ (46,459)	$ (59,674)
Weighted average shares outstanding:					
Basic	57,446,537	38,950,937	15,057,627	12,267,693	7,898,289
Diluted	65,048,892	38,950,937	15,057,627	12,267,693	7,898,289
Net income (loss) per share/unit:					
Basic	$ 0.05	$ (1.41)	$ (1.58)	$ (3.79)	$ (7.56)
Diluted	$ (0.34)	$ (1.41)	$ (1.58)	$ (3.79)	$ (7.56)

(in thousands)	As of December 31, 2018	2017	2016	2015	2014
Consolidated Balance Sheet Information					
Cash and cash equivalents	$ 16,645	$ 28,823	$ 14,202	$ 6,260	$ 16,815
Restricted cash, current	101	402	401	—	9,264
Restricted cash, non-current	300	150	307	457	1,548
Marketable securities	—	2,996	5,571	17,807	—
Total assets	18,360	36,810	29,702	38,409	33,391
Working capital	9,857	28,501	20,010	21,379	17,227
Total long term liabilities	6,965	32,325	5,215	—	—
Stockholders'/Members' equity (Deficiency in assets)	$ 3,856	$ (2,594)	$ 17,992	$ 30,336	$ 22,937

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

The following discussion and analysis of our financial condition and results of operations should be read together with our financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties and should be read together with the "Risk Factors" section of this Annual Report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

Business

We are a clinical-stage therapeutics company focused on developing innovative products 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 pulsatile nitric oxide delivery platform, INOpulse.

In 2016, we began developing INOpulse for the treatment of pulmonary hypertension associated with interstitial lung disease (PH-ILD), which includes PH associated with idiopathic pulmonary fibrosis (PH-IPF) as well as other pulmonary fibrosing diseases. During May 2017, we announced completion of our Phase 2 clinical trial using INOpulse therapy to treat PH-IPF. The clinical data showed that INOpulse was associated with clinically meaningful improvements in hemodynamics and exercise capacity in difficult-to-treat PH-IPF patients. The PH-IPF trial was a proof of concept study (n=4) designed to evaluate the ability of pulsed inhaled nitric oxide, or iNO, to provide selective vasodilation as well as to assess the potential for improvement in hemodynamics and exercise capacity in PH-IPF patients. The clinical trial met its primary endpoint showing an average of 15.3% increase in blood vessel volume ($p<0.001$) during acute inhalation of iNO as well as showing a significant association between ventilation and vasodilation, demonstrating the ability of INOpulse to provide selective vasodilation to the better ventilated areas of the lung. The trial showed consistent benefit in hemodynamics with a clinically meaningful average reduction of 14% in systolic pulmonary arterial pressure (sPAP) with acute exposure to iNO. The study assessed both the iNO 75 and iNO 30 dose, supporting iNO 30 as a potentially safe dose. During August 2017, we announced FDA acceptance of our IND for our Phase 2b (iNO-PF) clinical trial using INOpulse therapy in a broad population of patients with pulmonary fibrosis, or PF, at both low and intermediate/high risk of PH. In January 2018, we announced the first patient enrollment in our iNO-PF Phase 2b trial. In October 2018, we announced the enrollment completion of the planned 40 subjects, or cohort 1, in our iNO-PF study. In addition, we announced the expansion of the trial with the addition of cohort 2 and cohort 3, to evaluate a higher iNO 45 and iNO 75 dose as well as a longer 16 week evaluation period. In January 2019, we announced top-line results from cohort 1 of our iNO-PF study. The results showed statistically significant improvements in multiple clinically meaningful activity parameters as measured by a wearable medical-grade activity monitor: subjects on iNO demonstrated an increase of 8% in moderate activity versus a 26% decrease for subjects on placebo ($p=0.04$) and subjects on iNO showed no decline in their overall activity levels versus a 12% decline for subjects on placebo ($p=0.05$). In addition, clinically meaningful improvements were also demonstrated in the following key areas: subjects on iNO showed an increase of 15% in NT-ProBNP versus a 42% increase for subjects on placebo (NT-ProBNP is a peptide marker of right ventricular failure, with higher levels indicative of disease worsening) and subjects on iNO demonstrated improved oxygen saturation by 9% versus a worsening of 11% for placebo. In addition, iNO was well-tolerated with no safety concerns supporting the continuation into cohort 2. Actigraphy (medical wearable continuous activity monitoring) provides highly sensitive objective real-world physical activity data that correlates to clinically meaningful patient functional abilities and health outcomes. We are currently utilizing Actigraphy to evaluate multiple clinically meaningful activity parameters in the iNO-PF study. Actigraphy is currently being utilized as the primary endpoint in multiple late-stage clinical programs in various cardiopulmonary diseases such as heart failure and COPD.

We completed a randomized, placebo-controlled, double-blind, dose-confirmation Phase 2 clinical trial of INOpulse for pulmonary hypertension associated with chronic obstructive pulmonary disease, or PH-COPD, in July 2014. The results from this trial showed that iNO 30 was a potentially safe and effective dose for treatment of PH-COPD. Based on the results of this trial, we completed further Phase 2 testing to assess the targeted vasodilation provided by INOpulse in this patient population. We presented the results of this trial in September 2015 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 entitled "Pulmonary vascular effects of pulsed inhaled nitric oxide in COPD patients with pulmonary hypertension." During September 2017, we shared the results of our Phase 2a

PH-COPD study designed to evaluate the acute effects of pulsed inhaled nitric oxide, or iNO, on vasodilation as well as the chronic effect on hemodynamics and exercise tolerance. The trial showed a statistically significant increase (average 4.2%) in blood vessel volume on iNO compared to baseline (p=0.03), and a statistically significant correlation in Ventilation-Vasodilation (p=0.01). The chronic results demonstrated a statistically significant and clinically meaningful increase in 6MWD of 50.7m (p=0.04) as well as a decrease of 19.9% in systolic pulmonary arterial pressure (p=0.02), as compared to baseline. The therapy was well tolerated with no related safety concerns. In May 2018, we announced that the FDA concurred with the design of our planned Phase 2b study of INOpulse for treatment of PH-COPD. The study will assess the effect of INOpulse on various parameters including exercise capacity, right ventricular function and oxygen saturation, as well as other composite endpoints. We are currently evaluating alternatives for the funding and timing of this program.

In 2018, we also initiated development of INOpulse for the treatment of PH associated with Sarcoidosis (PH-Sarc). The study is a Phase 2a dose escalation design that will utilize right heart catheterization to assess the hemodynamic effect of INOpulse from a dose of iNO 30 to iNO 125 in PH-Sarc subjects. We have finalized the design of the study and are in the process of initiating sites, and expect to enroll our first subject in early 2019, with results expected later in 2019.

We initiated a Phase 3 clinical trial of INOpulse for PAH in June 2016. As agreed upon with the FDA, a pre-specified interim analysis was conducted by the Data Monitoring Committee, or DMC, in August 2018, after half of the planned subjects completed 16 weeks of blinded treatment. The data showed INOpulse provided clinically meaningful improvements in pulmonary vascular resistance (18%), cardiac output (0.7 L/min) and NT Pro-BNP. In addition, subjects on PAH background mono-therapy showed a 23 meter improvement in 6MWD, while subjects that were not on prostanoid background therapy showed a 17 meter improvement in 6MWD. However, the DMC determined that the overall change in 6MWD, the primary endpoint of the trial, was insufficient to support the continuation of the study. Accordingly, based on the DMC's recommendation, we have discontinued the trial. The trial results showed 6MWD was improved when subjects were on less background therapies and more patients deteriorated in 6MWD on placebo as compared to iNO. In addition, INOpulse was well tolerated and there were no safety concerns.

In addition, other potential indications for our INOpulse platform include: chronic thromboembolic PH, or CTEPH 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.

Financial Operations Overview

Prior to February 2014, we were a wholly-owned subsidiary of Ikaria, Inc. (a subsidiary of Mallinckrodt plc), or Ikaria. As part of an internal reorganization of Ikaria in October 2013, Ikaria transferred to us exclusive worldwide rights, with no royalty obligations, to develop and commercialize pulsed nitric oxide in PAH, PH-COPD and PH-IPF. 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, which we refer to as the Spin-Out, and as a result we became a stand-alone company. 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. In April 2018, we expanded the scope of our license from PH-IPF to PH in patients with Pulmonary Fibrosis (PH-PF), which includes idiopathic interstitial pneumonias, chronic hypersensitivity pneumonitis, occupational and environmental lung disease, with a royalty equal to 1% of net sales of any commercial products for PH-PF.

Revenue

To date, we have not generated any revenue from product sales and may not generate any revenue from product sales for the next several years, if ever. In the future, we may generate revenue from a combination of product sales, license fees and milestone payments in connection with strategic partnerships, and royalties from the sale of products developed under licenses

of our intellectual property. Our ability to generate revenue and become profitable depends primarily on our ability to successfully develop and commercialize or partner our product candidates as well as any product candidates we may advance in the future. We expect that any revenue we may generate will fluctuate from quarter to quarter as a result of the timing and amount of any payments we may receive under future partnerships, if any, and from sales of any products we successfully develop and commercialize, if any. If we fail to complete the development of any of our product candidates currently in clinical development or any future product candidates in a timely manner, or to obtain regulatory approval for such product candidates, our ability to generate future revenue, and our business, results of operations, financial condition and cash flows and future prospects would be materially adversely affected.

Research and Development Expenses

Research and development expenses consist of costs incurred in connection with the development of our product candidates, including upfront and development milestone payments, related to in-licensed product candidates and technologies.

Research and development expenses primarily consist of:

- employee-related expenses, including salary, benefits and stock-based compensation expense;
- expenses incurred under agreements with contract research organizations, investigative sites that conduct our clinical trials and consultants that conduct a portion of our pre-clinical studies;
- expenses relating to vendors in connection with research and development activities;
- the cost of acquiring and manufacturing clinical trial materials;
- facilities, depreciation and allocated expenses;
- lab supplies, reagents, active pharmaceutical ingredients and other direct and indirect costs in support of our pre-clinical and clinical activities;
- device development and drug manufacturing engineering;
- license fees related to in-licensed products and technology; and
- costs associated with non-clinical activities and regulatory approvals.

We expense research and development costs as incurred.

Conducting a significant amount of research and development is central to our business model. Product candidates in late stages of clinical development generally have higher development costs than those in earlier stages of clinical development primarily due to the increased size and duration of late-stage clinical trials. Subject to the availability of requisite financing, we plan to increase our research and development expenses for ongoing clinical programs for the foreseeable future as we seek to continue multiple clinical trials for our product candidates, including to potentially advance INOpulse for PH-COPD, and seek to identify additional early-stage product candidates.

We track external research and development expenses and personnel expenses on a program-by-program basis. We use our employee and infrastructure resources, including regulatory, quality, clinical development and clinical operations, across our clinical development programs and have included these expenses in research and development infrastructure. Research and development laboratory expenses are also not allocated to a specific program and are included in research and development infrastructure. Engineering activities related to INOpulse and the manufacture of cylinders related to INOpulse are included in INOpulse engineering.

INOpulse for PH-ILD

We initiated our clinical program in PH-ILD in 2016. During May 2017, we announced completion of our Phase 2 study using INOpulse therapy to treat PH-IPF. After reaching agreement with the FDA, we initiated and are currently conducting our Phase 2b trial in PH-ILD. In January 2018, we announced the first patient enrollment in our iNO-PF Phase 2b trial. In October 2018, we announced the enrollment completion of the planned 40 subjects, or cohort 1, in our iNO-PF study.

In addition, we announced the expansion of the trial with the addition of cohort 2 and cohort 3, to evaluate higher doses of iNO as well as a longer 16 week evaluation period. In January 2019, we announced top-line results from cohort 1 of our iNO-PF study. The results showed statistically significant improvements in multiple clinically meaningful activity parameters as measured by a wearable medical-grade activity monitor.

INOpulse for PH-COPD

We completed and received results from a randomized, placebo-controlled, double-blind, dose-confirmation Phase 2a clinical trial of INOpulse for PH-COPD in July 2014. During September 2017, we shared results of our Phase 2a PH-COPD study designed to evaluate the acute effects of pulsed inhaled nitric oxide, or iNO, on vasodilation as well as the chronic effect on hemodynamics and exercise tolerance. In May 2018, we announced that we reached agreement with the FDA on the design of our planned Phase 2b study of INOpulse for treatment of PH-COPD. We are currently evaluating alternatives for the funding and timing of this program.

INOpulse for PAH

We initiated a Phase 3 clinical trial of INOpulse for PAH in June 2016. As agreed upon with the FDA, a pre-specified interim analysis was conducted by the Data Monitoring Committee, or DMC, in August 2018, after half of the planned subjects completed 16 weeks of blinded treatment. The data showed INOpulse provided clinically meaningful improvements in pulmonary vascular resistance (18%), cardiac output (0.7 L/min) and NT Pro-BNP. In addition, subjects on PAH background mono-therapy showed a 23 meter improvement in 6MWD, while subjects that were not on prostanoid background therapy showed a 17 meter improvement in 6MWD. However, the DMC determined that the overall change in 6MWD, the primary endpoint of the trial, was insufficient to support the continuation of the study. Accordingly, based on the DMC's recommendation, we discontinued the trial in August 2018. The trial results showed 6MWD was improved when subjects were on less background therapies and more patients deteriorated in 6MWD on placebo as compared to iNO. In addition, INOpulse was well tolerated and there were no safety concerns.

Drug and Delivery System Costs

Drug and delivery system costs include cartridge procurement, cartridge filling, delivery system manufacturing and delivery system servicing. These costs relate to all indications that utilize the INOpulse delivery system. During the three months ended September 2017, we began to incur drug and delivery system costs for our Phase 2b study using INOpulse therapy in a broad population of patients with PF. Historically, drug and deliver system costs were primarily for our studies of INOpulse for PAH.

BCM

In December 2011, we initiated a clinical trial of BCM and completed enrollment in December 2014. Top-line results from the clinical trial were announced in July 2015. In July 2018, we informed BioLineRx Ltd., from whom we in-licensed the BCM technology, on our decision to discontinue further development and terminate the License and Commercialization Agreement.

Research and Development Infrastructure

We invest in regulatory, quality, clinical development and clinical operations activities, which are expensed as incurred. These activities primarily support our clinical development programs.

INOpulse Engineering

We have invested a significant amount of funds in INOpulse, which is configured to be highly portable and compatible with available modes of LTOT via nasal cannula delivery. Our Phase 2 clinical trials of INOpulse for PAH and INOpulse for PH-COPD utilized the first generation INOpulse DS/DS-C device. We believe our second generation INOpulse device, as well as a custom triple-lumen cannula, have significantly improved several characteristics of our INOpulse delivery system. We have also invested in design and engineering technology, through Ikaria, for the manufacture of our drug cartridges. In February 2015, we entered into an agreement with Flextronics Medical Sales and Marketing Ltd., a subsidiary of Flextronics

International Ltd., or Flex, to manufacture and service the INOpulse devices that we are using in our ongoing clinical trials of INOpulse for PH-ILD and PH-COPD.

General and Administrative Expenses

General and administrative expenses include salaries and costs related to executive, finance, and administrative support functions, patent filing, patent prosecution, professional fees for legal, insurance, consulting, investor relations, human resources, information technology and auditing and tax services not otherwise included in research and development expenses.

Results of Operations

Comparison of Years Ended December 31, 2018 and 2017

The following table summarizes our results of operations for the years ended December 31, 2018 and 2017, together with the changes in these items in dollars and as a percentage.

	Year Ended December 31,			
(Dollar amounts in thousands)	**2018**	**2017**	**$ Change**	**% Change**
Research and development expenses:				
PH-ILD and PH-COPD	2,147	478	1,669	349 %
PAH	$ 6,917	$ 6,117	$ 800	13 %
BCM	36	63	(27)	(43)%
Drug and delivery system costs	$ 4,856	$ 4,724	$ 132	3 %
Clinical programs	13,956	11,382	2,574	23 %
Research and development infrastructure	4,964	5,373	(409)	(8)%
INOpulse engineering	1,339	1,099	240	22 %
Total research and development expenses	20,259	17,854	2,405	13 %
General and administrative expenses	7,621	6,745	876	13 %
Loss from operations	(27,880)	(24,599)	(3,281)	13 %
Change in fair value of common stock warrant liability	24,877	(30,403)	55,280	(182)%
Interest and other income, net	378	184	194	105 %
Pre-tax loss	(2,625)	(54,818)	52,193	(95)%
Income tax benefit	(5,439)	—	(5,439)	N/A
Net income (loss)	$ 2,814	$ (54,818)	$ 57,632	(105)%

Total Operating Expenses. Total operating expenses for the year ended December 31, 2018 were $27.9 million compared to $24.6 million for the year ended December 31, 2017, an increase of $3.3 million, or 13%. This increase was primarily due to increased research and development expenses pertaining to our PH-ILD and PAH clinical trials as well as an increase in general and administration expenses.

Research and Development Expenses. Total research and development expenses for the year ended December 31, 2018 were $20.3 million compared to $17.9 million for the year ended December 31, 2017, an increase of $2.4 million, or 13%. Total research and development expenses consisted primarily of the following:

- PH-ILD and PH-COPD research and development expenses for the year ended December 31, 2018 were $2.1 million compared to $0.5 million for the year ended December 31, 2017, an increase of $1.7 million, or 349%. The increase was primarily due to start up fees associated with these programs and due to increased spending on our PH-ILD Phase 2b trial.

- PAH research and development expenses for the year ended December 31, 2018 were $6.9 million compared to $6.1 million for the year ended December 31, 2017, an increase of $0.8 million, or 13%. The increase was primarily driven by increased spending and closeout cost in the PAH Phase 3 trial.

- Drug and delivery system costs for the year ended December 31, 2018 were $4.9 million compared to $4.7 million for the year ended December 31, 2017, an increase of $0.2 million, or 3%. The increase was primarily due to material purchases for our PH-ILD trial partially offset by reduction in material purchases for our PAH trial.

- Research and development infrastructure expenses for the year ended December 31, 2018 were $5.0 million compared to $5.4 million for the year ended December 31, 2017, a decrease of $0.4 million, or 8%. The decrease was mainly due to decreased personnel costs.

- INOpulse engineering expenses for the year ended December 31, 2018 were $1.3 million compared to $1.1 million for the year ended December 31, 2017, an increase of $0.2 million, or 22%. The increase was primarily the result of an increase in consulting fees for the INOpulse system.

General and Administrative Expenses. General and administrative expenses for the year ended December 31, 2018 were $7.6 million compared to $6.7 million for the year ended December 31, 2017, an increase of $0.9 million, or 13%. The increase was primarily due to commercial, intellectual property, financial consulting expenses and stock based compensation expenses.

Change in fair value of common stock warrant liability. Change in fair value of common stock warrant liability for the year ended December 31, 2018 was income of $24.9 million compared to an expense of $30.4 million for the year ended December 31, 2017, a change of $55.3 million. The warrants were issued in November 2016 and May 2017 and the change in the liability fair value was primarily due to a change in our stock price and the timing of the warrants' issuance.

Income Tax Benefit. We had $5.4 million of income tax benefit for the year ended December 31, 2018 compared to zero for the year ended December 31, 2017. We have sold $61.5 million of state net operating losses, or NOLs, and $0.2 million of Research and Development credits under the State of New Jersey's Technology Business Tax Certificate Transfer Program in February 2018 for net proceeds of $5.3 million and, subject to program availability and state approval, have plans to sell additional NOLs and credits under the same program in following years as well.

Comparison of Years Ended December 31, 2017 and 2016

The following table summarizes our results of operations for the years ended December 31, 2017 and 2016, together with the changes in these items in dollars and as a percentage.

	Year Ended December 31,			
(Dollar amounts in thousands)	**2017**	**2016**	**$ Change**	**% Change**
Research and development expenses:				
PH-ILD and PH-COPD	$ 478	$ 185	$ 293	158 %
PAH	6,117	6,430	(313)	(5)%
BCM	63	425	(362)	(85)%
Drug and delivery system costs	4,724	3,017	1,707	57 %
Clinical programs	11,382	10,057	1,325	13 %
Research and development infrastructure	5,373	4,732	641	14 %
INOpulse engineering	1,099	1,861	(762)	(41)%
Total research and development expenses	17,854	16,650	1,204	7 %
General and administrative expenses	6,745	7,107	(362)	(5)%
Loss from operations	(24,599)	(23,757)	(842)	4 %
Change in fair value of common stock warrant liability	(30,403)	(590)	(29,813)	5,053 %
Interest and other income, net	184	95	89	94 %
Pre-tax loss	(54,818)	(24,252)	(30,566)	126 %
Income tax benefit	—	(438)	438	(100)%
Net loss	$ (54,818)	$ (23,814)	$ (31,004)	130 %

Total Operating Expenses. Total operating expenses for the year ended December 31, 2017 were $24.6 million compared to $23.8 million for the year ended December 31, 2016, an increase of $0.8 million, or 4%. This increase was primarily due to increased research and development expenses pertaining to drug and device costs and to our PH-COPD and PH-IPF clinical trials. The increase in research and development expenses was partially offset by a decrease in our general and administrative expenses.

Research and Development Expenses. Total research and development expenses for the year ended December 31, 2017 were $17.9 million compared to $16.7 million for the year ended December 31, 2016, an increase of $1.2 million, or 7%. Total research and development expenses consisted primarily of the following:

- PH-ILD and PH-COPD expenses for the year ended December 31, 2017 were $0.5 million compared to $0.2 million for the year ended December 31, 2016, an increase of $0.3 million or 158%. The increase was primarily due to clinical supplies and consulting fees to support the new Phase 2 clinical trials.

- PAH research and development expenses for the year ended December 31, 2017 were $6.1 million compared to $6.4 million for the year ended December 31, 2016, a decrease of $0.3 million, or 5%. The decrease was primarily due to completion of the Phase 2 clinical trial partially offset by a reversal of an accrual recorded in the year ended December 31, 2016 and increased costs for the Phase 3 clinical trial.

- BCM research and development expenses for the year ended December 31, 2017 were $0.1 million compared to $0.4 million for the year ended December 31, 2016, a decrease of $0.4 million, or 85%. The decrease was primarily due to the suspension of further clinical development of BCM following the PRESERVATION I results in July 2015.

- Drug and delivery system costs for the year ended December 31, 2017 were $4.7 million compared to $3.0 million for the year ended December 31, 2016, an increase of $1.7 million, or 57%. The increase was primarily due to the bulk purchase of cartridges in 2017 and an increase in cartridge fills to support the Phase 3 clinical trial. Starting in 2017, we began reporting drug and delivery system costs in a separate line in our Results of Operations discussion

due to the fact that these costs support multiple trials and at the time we incur these costs we do not know how to allocate them to a specific trial. In previous years, these expenses were related only to one trial.

- Research and development infrastructure expenses for the year ended December 31, 2017 were $5.4 million compared to $4.7 million for the year ended December 31, 2016, an increase of $0.6 million, or 14%. The increase was mainly due to increased personnel costs.

- INOpulse engineering expenses for the year ended December 31, 2017 were $1.1 million compared to $1.9 million for the year ended December 31, 2016, a decrease of $0.8 million, or 41%. The decrease was primarily the result of a reduction in development costs for the INOpulse system.

General and Administrative Expenses. General and administrative expenses for the year ended December 31, 2017 were $6.7 million compared to $7.1 million for the year ended December 31, 2016, a decrease of $0.4 million, or 5%. The decrease was primarily due to reduced personnel and consulting costs.

Change in fair value of common stock warrant liability. Change in fair value of common stock warrant liability for the year ended December 31, 2017 was $30.4 million compared to $0.6 million for the year ended December 31, 2016, a change of $29.8 million. The warrants were issued in November 2016 and in May 2017 and the increase was primarily due to an increase in our stock price and the timing of the warrants' issuance.

Income Tax Benefit. We had $0.0 million of income tax benefit for the year ended December 31, 2017 compared to $0.4 million for the year ended December 31, 2016 related to the sale of our state research and development tax credits in November 2016.

Liquidity and Capital Resources

In the course of our development activities, we have sustained operating losses and expect such losses to continue over the next several years. We expect to continue to incur significant expenses and operating losses for the foreseeable future as we continue to develop, conduct clinical trials and seek regulatory approval for our product candidates. Our primary uses of capital are, and we expect will continue to be, compensation and related expenses, third-party clinical research and development services, contract manufacturing services, laboratory and related supplies, clinical costs, legal and other regulatory expenses and general overhead costs.

If we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses. We do not have a sales, marketing, manufacture or distribution infrastructure for a pharmaceutical product. To develop a commercial infrastructure, we will have to invest financial and management resources, some of which would have to be deployed prior to having any certainty of marketing approval.

We had cash and cash equivalents of $16.6 million as of December 31, 2018. Our existing cash and cash equivalents and marketable securities as of December 31, 2018 will be used primarily to complete the Phase 2b trial of INOpulse for PH-ILD and to complete the dose escalation study for PH-Sarc.We expect to report top-line results for these trials during 2019.

On October 25, 2016, we filed a registration statement on Form S-1 with the SEC, which as amended became effective on November 22, 2016. On November 29, 2016, we completed the sale of 17,142,858 Class A Units consisting of an aggregate of 17,142,858 shares of our common stock and warrants exercisable for up to 17,142,858 shares of our common stock at a price of $0.70 per Unit, or the Secondary Offering, resulting in net proceeds of $10.9 million, after deducting placement fees of $0.8 million and offering costs of $0.3 million. Each warrant has an exercise price per full share of common stock equal to $0.80, is immediately exercisable and expires five years from the date on which such warrant becomes exercisable. The warrants require cash settlement by us under certain situations. During the years ended December 31, 2018 and 2017, we received proceeds of $0.2 million for the exercise of 239,824 warrants and $2.3 million for exercise of 2,872,585 warrants, respectively.

On May 9, 2017, we entered into a Securities Purchase Agreement, or the Purchase Agreement, with a single institutional investor for the sale of 2,000,000 shares of our common stock at a purchase price of $1.50 per share and warrants to purchase up to an aggregate of 1,000,000 shares of our common stock, or the Direct Offering. The warrants became exercisable commencing six months from the issuance date at an exercise price equal to $1.50 per full share of common stock, subject to adjustments as provided under the terms of the warrants. The warrants are exercisable for five years from the initial exercise date. In addition, the Company issued to the placement agent of the Direct Offering, warrants to purchase up to 60,000 shares. The placement agent warrants have substantially the same terms as the warrants issued to the investor, except that the placement agent warrants have an exercise price equal to $1.875 and will be exercisable for five years from the date of the

closing of this offering. The closing of the sales of these securities under the Purchase Agreement occurred on May 15, 2017. The aggregate gross and net proceeds for the Direct Offering were $3.0 million and $2.7 million, respectively.

On September 26, 2017, we entered into a Securities Purchase Agreement, or the PIPE Purchase Agreement, pursuant to which we sold an aggregate of 19,449,834 shares of our common stock at a purchase price of $1.205 per share and warrants to purchase up to an aggregate of 19,449,834 shares of our common stock, or the PIPE Offering. The warrants became exercisable commencing six months from the issuance date at an exercise price equal to $1.2420 per full share of common stock, subject to adjustments as provided under the terms of the warrants. The warrants are exercisable for five years from the initial exercise date. The closing of the sales of these securities under the Purchase Agreement occurred on September 29, 2017. The aggregate gross and net proceeds for the PIPE Offering were $23.4 million and $22.8 million, respectively.

On June 25, 2018, we filed a shelf registration statement on Form S-3 with the SEC, which became effective on July 6, 2018. The shelf registration allows us to issue, from time to time at prices and on terms to be determined prior to the time of any such offering, up to $100 million of any combination of common stock, preferred stock, debt securities, warrants and rights, either individually or in units.

On January 25, 2019, we completed the sale of 10,000,000 shares of our common stock at a public offering price of $0.70 per share, resulting in net proceeds of approximately $6.2 million, after deducting placement fees of $0.5 million and offering costs of $0.3 million.

We continue to pursue potential sources of funding, including equity financing.

We have evaluated whether there are any conditions and events, considered in the aggregate, that raise substantial doubt about our ability to continue as a going concern within one year beyond the filing of this Annual Report on Form 10-K.

We believe that our existing cash and cash equivalents and marketable securities as of December 31, 2018, the proceeds from the January 25, 2019 public offering and proceeds that will become available to us upon sale of our state NOLs, and research and development (R&D) tax credits under the State of New Jersey's Technology Business Tax Certificate Transfer Program will be sufficient to satisfy our operating cash needs for at least one year after the filing of this Annual Report on Form 10-K.

The Technology Business Tax Certificate Transfer Program enables qualified, unprofitable New Jersey based technology or biotechnology companies to sell a percentage of NOL and R&D tax credits to unrelated profitable corporations, subject to meeting certain eligibility criteria. Based on consideration of various factors, including application processing time and past trend of benefits made available under the program, we believe that it is probable that our plans to sell our NOLs can be effectively implemented to address our short term financial needs. We sold $61.5 million of state NOLs and $0.2 million of R&D credits under the State of New Jersey's Technology Business Tax Certificate Transfer Program in February 2018 for net proceeds of $5.3 million and we sold an additional $20 million of state NOLs for net proceeds of $1.7M in January 2019. Subject to program availability and state approval, we also plan to sell additional NOLs and credits under the same program later in 2019. The proceeds from such sales are recorded as Income tax benefit when sales occur or proceeds are received.

We have based our estimates on assumptions that may prove to be wrong, and we may exhaust our capital resources sooner than we expect. In addition, the process of testing product candidates in clinical trials is costly, and the timing of progress in clinical trials is uncertain. Because our product candidates are in clinical development and the outcome of these efforts is uncertain, we cannot estimate the actual amounts that will be necessary to successfully complete the development and commercialization of our product candidates or whether, or when, we may achieve profitability. Our future capital requirements will depend on many factors, including:

- progress and cost of our clinical trials and other research and development activities;
- our ability to manufacture sufficient supply of our product candidates and the costs thereof;
- the cost and timing of seeking regulatory approvals;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution for any of our product candidates for which we receive marketing approval;
- the number and development requirements of any other product candidates we pursue;
- our ability to enter into collaborative agreements and achieve milestones under those agreements;

- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- the cost of filing, prosecuting, defending and enforcing patent applications, claims, patents and other intellectual property rights; and
- the extent to which we acquire or in-license other products and technologies.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity and debt offerings, sales of state NOL and R&D credits, existing working capital and funding from potential future collaboration arrangements. To the extent that we raise additional capital through the future sale of equity or debt, the ownership interest of our existing stockholders will be diluted, and the terms of such securities may include liquidation or other preferences or rights such as anti-dilution rights that adversely affect the rights of our existing stockholders. If we raise additional funds through strategic partnerships in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. In addition, the timing of when existing and new capital resources are used and received may not align with the period of time evaluated by management for going concern purposes such that management may be required to conclude that substantial doubt about our ability to continue as a going concern in accordance with relevant accounting guidance may exist in future periods.

Cash Flows

The following table summarizes our cash flows for the years ended December 31, 2018, 2017 and 2016:

	Year Ended December 31,		
(Dollar amounts in thousands)	**2018**	**2017**	**2016**
Operating activities	$ (15,495)	$ (15,896)	$ (17,213)
Investing activities	3,000	2,577	12,199
Financing activities	166	27,784	13,207
Net change in cash, cash equivalents and restricted cash	$ (12,329)	$ 14,465	$ 8,193

Net Cash Used in Operating Activities

Cash used in operating activities for the year ended December 31, 2018 was $15.5 million compared to $15.9 million for the year ended December 31, 2017, a decrease of $0.4 million, or 3%. The decrease in cash used in operating activities was primarily due to changes in operating assets and liabilities.

Cash used in operating activities for the year ended December 31, 2017 was $15.9 million compared to $17.2 million for the year ended December 31, 2016, a decrease of $1.3 million, or 8%. The decrease in cash used in operating activities was primarily due to changes in operating assets and liabilities.

Net Cash Provided by Investing Activities

Cash provided by investing activities for the year ended December 31, 2018 was $3.0 million compared to $2.6 million for the year ended December 31, 2017 which mostly represented net activity related to purchase and sale of our marketable securities.

Cash provided by investing activities for the year ended December 31, 2017 was $2.6 million compared to $12.2 million for the year ended December 31, 2016, which mostly represented net activity related to purchase and sale of our marketable securities.

Net Cash Provided by Financing Activities

Cash provided by financing activities for the year ended December 31, 2018 was $0.2 million, which primarily included the proceeds from warrant exercises, compared to $27.8 million for the year ended December 31, 2017, which included the net proceeds from the PIPE Offering, Direct Offering and proceeds from exercise of warrants.

Cash provided by financing activities for the year ended December 31, 2017 was $27.8 million, which included the net proceeds from our PIPE Offering, Direct Offering and proceeds from exercise of warrants, compared to $13.2 million for the year ended December 31, 2016, which included the net proceeds from our ATM Offering and Secondary Offering.

Contractual Obligations and Commitments

The following is a summary of our long-term contractual cash obligations as of December 31, 2018 (in thousands):

	Payments Due by Period ($)			
Contractual Obligations	**Total**	**Less than 1 year**	**1 to 3 years**	**3 to 5 years**
Operating Lease Obligations(1)	$ 2,848	$ 653	$ 1,338	$ 857
Total	$ 2,848	$ 653	$ 1,338	$ 857

(1) Operating lease obligations include the lease agreement we entered into on August 6, 2015 for office space in Warren, New Jersey.

Royalty payments and success-based milestones associated with our license and supply agreements with Ikaria have not been included in the above table of contractual obligations as we cannot reasonably estimate if or when they will occur.

In the course of our normal business operations, we also enter into agreements with suppliers, contract service providers and others to assist in the performance of our research and development and manufacturing activities. We can elect to discontinue the work under these contracts and purchase orders at any time with notice, and such contracts and purchase orders do not contain minimum purchase obligations.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable Securities and Exchange Commission rules.

Critical Accounting Policies and Significant Judgments and Estimates

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

While our significant accounting policies are described in Note 2 of the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our financial statements.

Research and Development Expense

Research and development costs are expensed as incurred. These expenses include the costs of our proprietary research and development efforts, as well as costs incurred in connection with certain licensing arrangements. Upfront and milestone payments made to third parties in connection with research and development collaborations are expensed as incurred up to the

point of regulatory approval. Payments made to third parties upon or subsequent to regulatory approval are capitalized and amortized over the remaining useful life of the related product. We expense the cost of purchased technology and equipment in the period of purchase if we believe that the technology or equipment has not demonstrated technological feasibility and does not have an alternative future use. Nonrefundable advance payments for goods or services that will be used or rendered for future research and development activities are deferred and are recognized as research and development expense as the related goods are delivered or the related services are performed.

As part of the process of preparing our financial statements, we are required to estimate a portion of our prepaid and accrued research expenses. This process involves reviewing open contracts and purchase orders, communicating with applicable personnel and third party service providers to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. We make such estimates of our incurred research and development expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Examples of estimated prepaid and accrued research and development expenses include:

- fees paid to contract research organizations in connection with clinical trials;
- fees paid to investigative sites in connection with clinical trials; and
- fees paid to contract manufacturers in connection with the production of clinical trial materials.

We base our expenses related to research and development and clinical trials on actual costs incurred in addition to our estimates of the services received and efforts expended pursuant to contracts with multiple third parties, including research institutions and contract research organizations that conduct and manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing the research and development service fees, we consider the terms of each agreement, the time period over which the services will be performed and the level of effort required to complete the service. If the actual timing of the performance of the services or the level of effort varies from our estimate, we adjust the accrual accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low in any particular period.

It is difficult to determine with certainty the duration and completion costs of our current or any future pre-clinical programs and any of our current or future clinical trials and any future product candidates we may advance, or if, when or to what extent we will generate revenue from the commercialization and sale of any of our product candidates that obtain regulatory approval. We may never succeed in achieving regulatory approval for any of our product candidates. The duration, costs and timing of clinical trials and development of our product candidates will depend on a variety of factors, including the uncertainties of any future clinical trials and pre-clinical studies, uncertainties in clinical trial enrollment rate and significant and changing government regulation. In addition, the probability of success for each product candidate will depend on numerous factors, including competition, manufacturing capability and commercial viability. A change in the outcome of any of these variables with respect to the development of a product candidate could change significantly the costs and timing associated with the development of that product candidate. For example, if the FDA or other regulatory authority were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of clinical development of a product candidate, or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time with respect to the development of that product candidate. We will determine which programs to pursue and how much to fund each program in response to the scientific and clinical success of each product candidate, as well as an assessment of each product candidate's commercial potential, including the likelihood of regulatory approval on a timely basis.

Common Stock Warrant Liability

We account for common stock warrants issued as freestanding instruments in accordance with applicable accounting guidance provided in Accounting Standards Codification , or ASC Topic 480, *Distinguishing Liabilities From Equity* , as either liabilities or as equity instruments depending on the specific terms of the warrant agreement. We classify warrant liability on the consolidated balance sheet as current liabilities, which are revalued at each balance sheet date subsequent to the initial issuance. Changes in the fair value of the warrants are reflected in the consolidated statement of operations as "Change in fair

value of common stock warrant liability." We use the Black-Scholes-Merton pricing model to value the related warrant liability. Certain assumptions used in the model include expected volatility, dividend yield and risk-free interest rate. Refer to Note 6 of the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for a detailed description of our accounting for warrants.

Stock-Based Compensation

We issue stock based awards to employees and non-employees in the form of stock options, restricted stock awards, or RSAs, and may issue restricted stock units, or RSUs.

We account for our stock-based compensation in accordance with ASC Topic 718 *Compensation- Stock Compensation*, which establishes accounting for share-based awards, including stock options and restricted stock, exchanged for services and requires companies to expense the estimated fair value of these awards over the requisite service period. We recognize stock-based compensation expense in operations based on the fair value of the award on the date of the grant. The resulting compensation expense is recognized on a straight-line basis over the requisite service period or sooner if the awards immediately vest. We use the Black-Scholes-Merton option pricing model to value our stock option awards. Refer to Note 8 of the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for a detailed description of our accounting for stock-based compensation.

Recently Issued Accounting Standards

Adopted

In November 2016, the FASB issued ASU 2016-18 "Statement of Cash Flows: Restricted Cash," which eliminates the diversity in practice related to the inclusion of restricted cash in the statement of cash flows by requiring that a statement of cash flows include the change during the period in restricted cash when reconciling beginning-of-period and end-of-period total amounts shown on the statement of cash flows. The Company retrospectively adopted ASU 2016-18 during the quarter ended March 31, 2018 by including restricted cash with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows.

Not Yet Adopted

In February 2016, the FASB issued ASU No. 2016-02, "Leases" (ASU 2016-02) which provides accounting guidance for both lessee and lessor accounting models. Among other things, lessees will recognize a right-of-use asset and a lease liability for leases with a duration of greater than one year. For income statement purposes, ASU 2016-02 will require leases to be classified as either an operating or finance lease. Operating leases will result in straight-line expense while finance leases will result in a front-loaded expense pattern. The new standard will be effective for us on January 1, 2019. In July 2018, the FASB issued ASU No. 2018-11, "Leases" (ASU 2018-11), which offers a transition option to entities adopting the new lease standard. Under the transition option, entities can elect to apply the new guidance using a modified retrospective approach at the beginning of the year in which the new lease standard is adopted, rather than to the earliest comparative period presented in their financial statements. We will adopt the standard using the modified retrospective method. We continue to evaluate the impact of ASU 2016-02 on its consolidated financial statements. The recognition of lease liabilities and corresponding ROU assets is expected to have a material impact on our consolidated balance sheet. We estimate that it will record approximately $2.6 million of lease liabilities and $2.3 million of ROU assets as of January 1, 2019, the difference representing previously recorded lease-related liabilities. We do not believe the adoption of this standard will have a material impact on its consolidated statements of operations, stockholders' equity (deficiency in assets) or cash flows. Refer to Note 12 of the financial statement, Commitments and Contingencies, for further information on our existing leases.

In August 2018, the FASB issued ASU 2018-13, "Fair Value Measurement (Topic 820) - Disclosure Framework - Changes to the Disclosure Requirements for Fair Value Measurement", which eliminates, modifies and adds certain disclosure on fair value measurements. This standard will be effective for fiscal years beginning after December 15, 2019, including interim periods within those fiscal years. The Company is assessing ASU 2018-03's impact and will adopt it when effective.

JOBS Act

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 $1.07 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 the last business day of our most recently completed second fiscal quarter. 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 our filings with the SEC. 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. 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.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

We are exposed to market risk related to changes in interest rates. As of December 31, 2018, we had cash and cash equivalents of $16.6 million, consisting primarily of demand deposits with U.S. banking institutions. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in cash and cash equivalents. Due to the nature of our deposits and the low risk profile of our investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our deposits.

Item 8. Financial Statements and Supplementary Data

Index to Financial Statements

	Page
Report of Independent Registered Public Accounting Firm	84
Consolidated Balance Sheets as of December 31, 2018 and 2017	85
Consolidated Statements of Operations for the years ended December 31, 2018 , 2017 and 2016	86
Consolidated Statements of Comprehensive Income (Loss) for the years ended December 31, 2018, 2017 and 2016	87
Consolidated Statement of Changes in Stockholders'/Members' Equity (Deficiency in Assets) for the years ended December 31, 2018, 2017 and 2016	88
Consolidated Statements of Cash Flows for the years ended December 31, 2018, 2017 and 2016	89
Notes to Consolidated Financial Statements	90

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Bellerophon Therapeutics, Inc.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Bellerophon Therapeutics, Inc. and subsidiaries (the Company) as of December 31, 2018 and 2017, the related consolidated statements of operations, comprehensive income (loss), changes in stockholders' equity (deficiency in assets), and cash flows for each of the years in the three-year period ended December 31, 2018, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

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

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

/s/ KPMG LLP

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

Short Hills, New Jersey
March 14, 2019

BELLEROPHON THERAPEUTICS, INC.

Consolidated Balance Sheets

(Amounts in thousands, except share and per share data)

	December 31, 2018	December 31, 2017
Assets		
Current assets:		
Cash and cash equivalents	$ 16,645	$ 28,823
Restricted cash	101	402
Marketable securities	—	2,996
Prepaid expenses and other current assets	650	3,359
Total current assets	17,396	35,580
Restricted cash, non-current	300	150
Other non-current assets	—	54
Property and equipment, net	664	1,026
Total assets	$ 18,360	$ 36,810
Liabilities and Stockholders' Equity (Deficiency in Assets)		
Current liabilities:		
Accounts payable	$ 2,755	$ 3,853
Accrued research and development	3,771	1,785
Accrued expenses	1,013	1,441
Total current liabilities	7,539	7,079
Common stock warrant liability	6,965	32,325
Total liabilities	14,504	39,404
Commitments and contingencies (Note 12)		
Stockholders' equity (Deficiency in assets):		
Common stock, $0.01 par value per share; 200,000,000 and 125,000,000 shares authorized and 58,679,492 and 56,899,353 shares issued and outstanding at December 31, 2018 and 2017, respectively, 289,269 shares paid for and to be issued at December 31, 2017	587	569
Preferred stock, $0.01 par value per share; 5,000,000 shares authorized, zero shares issued and outstanding at December 31, 2018 and 2017	—	—
Additional paid-in capital	179,765	176,151
Accumulated other comprehensive loss	—	(4)
Accumulated deficit	(176,496)	(179,310)
Total stockholders' equity (deficiency in assets)	3,856	(2,594)
Total liabilities and stockholders' equity (deficiency in assets)	$ 18,360	$ 36,810

The accompanying notes are an integral part of these consolidated financial statements.

BELLEROPHON THERAPEUTICS, INC.

Consolidated Statements of Operations

(Amounts in thousands, except share and per share data)

	Year Ended December 31,		
	2018	2017	2016
Operating expenses:			
Research and development	$ 20,259	$ 17,854	$ 16,650
General and administrative	7,621	6,745	7,107
Total operating expenses	27,880	24,599	23,757
Loss from operations	(27,880)	(24,599)	(23,757)
Change in fair value of common stock warrant liability	24,877	(30,403)	(590)
Interest and other income, net	378	184	95
Pre-tax loss	(2,625)	(54,818)	(24,252)
Income tax benefit	(5,439)	—	(438)
Net income (loss)	$ 2,814	$ (54,818)	$ (23,814)
Weighted average shares outstanding:			
Basic	57,446,537	38,950,937	15,057,627
Diluted	65,048,892	38,950,937	15,057,627
Net income (loss) per share:			
Basic	$ 0.05	$ (1.41)	$ (1.58)
Diluted	$ (0.34)	$ (1.41)	$ (1.58)

The accompanying notes are an integral part of these consolidated financial statements.

BELLEROPHON THERAPEUTICS, INC.

Consolidated Statements of Comprehensive Income (Loss)
(in thousands)

	Year Ended December 31,		
	2018	2017	2016
Net income (loss)	$ 2,814	$ (54,818)	$ (23,814)
Other comprehensive income (loss)			
Unrealized gains (losses) on available-for-sale marketable securities	$ 4	$ (4)	$ 19
Total other comprehensive income (loss)	$ 4	$ (4)	$ 19
Comprehensive income (loss)	$ 2,818	$ (54,822)	$ (23,795)

The accompanying notes are an integral part of these consolidated financial statements.

BELLEROPHON THERAPEUTICS, INC.

Consolidated Statements of Changes in Stockholders' Equity (Deficiency in Assets)
(Amounts in thousands except share and per share data)

	Common Stock					
	Shares	Amount	Additional Paid in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders'/Members' Equity (Deficiency in Assets)
Balance at December 31, 2015	13,130,800	$ 131	$ 130,902	$ (19)	$ (100,678)	30,336
Net loss	—	—	—	—	(23,814)	(23,814)
Other comprehensive income	—	—	—	19	—	19
Sale of common stock in ATM offering, net of offering expenses of $134	1,025,793	10	2,099	—	—	2,109
Sale of common stock in Secondary Offering, net of offering expenses of $662	17,142,858	172	6,540	—	—	6,712
Stock-based compensation	403,173	4	2,626	—	—	2,630
Balance at December 31, 2016	31,702,624	$ 317	$ 142,167	$ —	$ (124,492)	$ 17,992
Net loss	—	—	—	—	(54,818)	(54,818)
Other comprehensive loss	—	—	—	(4)	—	(4)
Sale of common stock and warrants in PIPE Offering, net of offering expenses of $677	19,449,834	194	22,565	—	—	22,759
Sale of common stock in Direct Offering, net of offering expenses of $187	2,000,000	20	1,675	—	—	1,695
Warrant exercises - shares exclude 289,269 shares paid for but not issued in 2017	2,872,585	29	6,912	—	—	6,941
Stock-based compensation	874,310	9	2,832	—	—	2,841
Balance at December 31, 2017	56,899,353	$ 569	$ 176,151	$ (4)	$ (179,310)	$ (2,594)
Net income	—	—	—	—	2,814	2,814
Other comprehensive income	—	—	—	4	—	4
Warrant exercises - shares include 289,269 shares paid for in 2017 and issued in 2018	529,093	5	668	—	—	673
Exercise of stock options	5,875	—	4	—	—	4
Stock-based compensation	1,245,171	13	2,942	—	—	2,955
Balance at December 31, 2018	58,679,492	$ 587	$ 179,765	$ —	$ (176,496)	$ 3,856

The accompanying notes are an integral part of these consolidated financial statements.

BELLEROPHON THERAPEUTICS, INC.

Consolidated Statements of Cash Flows

(Amounts in thousands)

	Year Ended December,		
	2018	**2017**	**2016**
Cash flows from operating activities:			
Net income (loss)	$ 2,814	$ (54,818)	$ (23,814)
Adjustments to reconcile net income (loss) to net cash used in operating activities:			
Depreciation	362	373	400
Stock-based compensation	2,955	2,841	2,758
Change in fair value of common stock warrant liability	(24,877)	30,403	590
Accretion and amortization of discounts and premiums on marketable securities, net	—	(6)	34
Issuance costs attributable to common stock warrant liability	—	111	415
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	2,709	2,972	(946)
Other non-current assets	54	1,437	5,210
Accounts payable, accrued research and development and accrued expenses	488	791	(1,860)
Net cash used in operating activities	(15,495)	(15,896)	(17,213)
Cash flows from investing activities:			
Capital expenditures	—	—	(22)
Purchase of marketable securities	—	(5,981)	—
Proceeds from sale of marketable securities	3,000	8,558	12,221
Net cash provided by investing activities	3,000	2,577	12,199
Cash flows from financing activities:			
Proceeds received from exercise of warrants	190	2,299	—
Proceeds received from exercise of options	4	—	—
Proceeds from sale of common stock in ATM Offering, net of commissions and offering expenses	—	—	2,144
Proceeds from exercise of warrants pending issuance of common shares	—	231	—
Proceeds from sale of Units in Secondary Offering, net of commissions and offering expenses	—	(235)	11,191
Proceeds from sale of Units in PIPE Offering, net of offering expenses	(28)	22,759	—
Proceeds from sale of Units in Direct Offering, net of commissions and offering expenses	—	2,730	—
Tax withholding payments for stock compensation	—	—	(128)
Net cash provided by financing activities	166	27,784	13,207
Net change in cash, cash equivalents and restricted cash	(12,329)	14,465	8,193
Cash, cash equivalents and restricted cash at beginning of year	29,375	14,910	6,717
Cash, cash equivalents and restricted cash at end of year	$ 17,046	$ 29,375	$ 14,910
Non-cash investing activities:			
Change in unrealized holding gains on marketable securities, net	$ 4	$ (4)	$ 19
Non-cash financing activities:			
Conversion of warrant liability to common stock upon exercise of warrants	$ 483	$ 4,411	$ —
Unpaid expenses related to offerings	$ —	$ 28	$ 304

The accompanying notes are an integral part of these consolidated financial statements.

BELLEROPHON THERAPEUTICS, INC.

Notes to Consolidated Financial Statements

(1) Organization and Nature of the Business

Bellerophon Therapeutics, Inc., or the Company, is a clinical-stage therapeutics company focused on developing innovative products that address significant unmet medical needs in the treatment of cardiopulmonary diseases. The focus of the Company's clinical program is the continued development of its nitric oxide therapy for patients with pulmonary hypertension, or PH, using its proprietary delivery system, INOpulse. The Company has 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.

The Company's business is subject to significant risks and uncertainties, including but not limited to:

- The risk that the Company will not achieve success in its research and development efforts, including clinical trials conducted by it or its potential collaborative partners.
- The expectation that the Company will experience operating losses for the next several years.
- Decisions by regulatory authorities regarding whether and when to approve the Company's regulatory applications as well as their decisions regarding labeling and other matters which could affect the commercial potential of the Company's products or product candidates.
- The risk that the Company will fail to obtain adequate financing to meet its future operational and capital needs.
- The risk that the Company will be unable to obtain additional funds on a timely basis and hence there will be substantial doubt about its ability to continue as a going concern.
- The risk that key personnel will leave the Company and/or that the Company will be unable to recruit and retain senior level officers to manage its business.

(2) Summary of Significant Accounting Policies

(a) Basis of Presentation

The financial statements have been prepared in accordance with U.S. generally accepted accounting principles or GAAP. Intercompany balances and transactions have been eliminated. The Company operates in one reportable segment and solely within the United States. Accordingly, no segment or geographic information has been presented.

The preparation of financial statements requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of costs and expenses during the reporting period, including prepaid and accrued research and development expenses, stock-based compensation, common stock warrant liability and income taxes. Actual results could differ from those estimates.

(b) Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity date of three months or less to be cash equivalents. All investments with maturities of greater than three months from date of purchase are classified as available-for-sale marketable securities.

(c) Stock-Based Compensation

The Company accounts for its stock-based compensation in accordance with applicable accounting guidance which establishes accounting for share-based awards, including stock options and restricted stock, exchanged for services and requires companies to expense the estimated fair value of these awards over the requisite service period. The Company recognizes stock-based compensation expense in operations based on the fair value of the award on the date of the grant. The resulting

compensation expense, less estimated forfeitures, is recognized on a straight-line basis over the requisite service period or sooner if the awards immediately vest. The Company determines the fair value of stock options issued using a Black-Scholes-Merton option pricing model. Certain assumptions used in the model include expected volatility, dividend yield, risk-free interest rate, estimated forfeitures and expected term. For restricted stock, the fair value is the closing market price per share on the grant date. See Note 8 - *Stock-Based Compensation* for a description of these assumptions.

(d) Common Stock Warrant Liability

The Company accounts for common stock warrants issued as freestanding instruments in accordance with applicable accounting guidance as either liabilities or as equity instruments depending on the specific terms of the warrant agreement. The Company classifies warrant liability on the consolidated balance sheet based on the warrants' terms as long-term liabilities, which are revalued at each balance sheet date subsequent to the initial issuance. Changes in the fair value of the warrants are reflected in the consolidated statement of operations as “Change in fair value of common stock warrant liability.” The Company uses the Black-Scholes-Merton pricing model to value the related warrant liability. Certain assumptions used in the model include expected volatility, dividend yield and risk-free interest rate. See Note 7 - *Fair Value Measurements* for a description of these assumptions.

(e) Income Taxes

The Company uses the asset and liability approach to account for income taxes as required by applicable accounting guidance, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases. Valuation allowances are provided when necessary to reduce deferred tax assets to the amount expected to be realized, on a more likely than not basis. The Company recognizes the benefit of an uncertain tax position that it has taken or expects to take on income tax returns it files if such tax position is more likely than not to be sustained on examination by the taxing authorities, based on the technical merits of the position. These tax benefits are measured based on the largest benefit that has a greater than 50% likelihood of being realized upon ultimate resolution.

(f) Marketable Securities

Unrealized gains and losses are reported as accumulated other comprehensive income (loss) , except for losses from impairments which are determined to be other-than-temporary. Realized gains and losses, and declines in value judged to be other-than-temporary on available-for-sale securities are included in the determination of net loss and are included in interest and other income, at which time the average cost basis of these securities are adjusted to fair value. Fair values are based on quoted market prices at the reporting date. Interest on available-for-sale securities is included in interest and other income.

(g) Research and Development Expense

Research and development costs are expensed as incurred. These expenses include the costs of the Company’s proprietary research and development efforts, as well as costs incurred in connection with certain licensing arrangements. Upfront and milestone payments made to third parties in connection with research and development collaborations are expensed as incurred up to the point of regulatory approval. Payments made to third parties upon or subsequent to regulatory approval are capitalized and amortized over the remaining useful life of the related product. The Company expenses the cost of purchased technology and equipment in the period of purchase if it believes that the technology or equipment has not demonstrated technological feasibility and it does not have an alternative future use. Nonrefundable advance payments for goods or services that will be used or rendered for future research and development activities are deferred and are recognized as research and development expense as the related goods are delivered or the related services are performed.

(h) New Accounting Pronouncements

Adopted

In November 2016, the FASB issued ASU 2016-18 “Statement of Cash Flows: Restricted Cash,” which eliminates the diversity in practice related to the inclusion of restricted cash in the statement of cash flows by requiring that a statement of cash flows include the change during the period in restricted cash when reconciling beginning-of-period and end-of-period total amounts shown on the statement of cash flows. The Company retrospectively adopted ASU 2016-18 during the quarter ended

March 31, 2018 by including restricted cash with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows.

Not Yet Adopted

In February 2016, the FASB issued ASU No. 2016-02, “Leases” (ASU 2016-02) which provides accounting guidance for both lessee and lessor accounting models. Among other things, lessees will recognize a right-of-use asset and a lease liability for leases with a duration of greater than one year. For income statement purposes, ASU 2016-02 will require leases to be classified as either an operating or finance lease. Operating leases will result in straight-line expense while finance leases will result in a front-loaded expense pattern. The new standard will be effective for us on January 1, 2019. In July 2018, the FASB issued Accounting Standards Update No. 2018-11, “Leases” (ASU 2018-11), which offers a transition option to entities adopting the new lease standard. Under the transition option, entities can elect to apply the new guidance using a modified retrospective approach at the beginning of the year in which the new lease standard is adopted, rather than to the earliest comparative period presented in their financial statements. The Company will adopt the standard using the modified retrospective method. The Company continues to evaluate the impact of ASU 2016-02 on its consolidated financial statements. The recognition of lease liabilities and corresponding ROU assets is expected to have a material impact on the Company’s consolidated balance sheet. The Company estimates that it will record approximately $2.6 million of lease liabilities and $2.3 million of ROU assets as of January 1, 2019, the difference representing previously recorded lease-related liabilities. The Company does not believe the adoption of this standard will have a material impact on its consolidated statements of operations, stockholders’ equity (deficiency in assets) or cash flows. Refer to Note 12, *Commitments and Contingencies*, for further information on the Company’s existing leases.

In August 2018, the FASB issued ASU 2018-13, “Fair Value Measurement (Topic 820) - Disclosure Framework - Changes to the Disclosure Requirements for Fair Value Measurement”, which eliminates, modifies and adds certain disclosure on fair value measurements. This standard will be effective for fiscal years beginning after December 15, 2019, including interim periods within those fiscal years. The Company is assessing ASU 2018-03’s impact and will adopt it when effective.

(3) Liquidity

In the course of its development activities, the Company has sustained operating losses and expects such losses to continue over the next several years. The Company expects to continue to incur significant expenses and operating losses for the foreseeable future as it continues the development and clinical trials of, and seek regulatory approval for, its product candidates. The Company's primary uses of capital are, and it expects will continue to be, compensation and related expenses, third-party clinical research and development services, contract manufacturing services, laboratory and related supplies, clinical costs, legal and other regulatory expenses and general overhead costs.

If the Company obtains regulatory approval for any of its product candidates, the Company expects to incur significant commercialization expenses. The Company does not have a sales, marketing, manufacturing or distribution infrastructure for a pharmaceutical product. To develop a commercial infrastructure, the Company will have to invest financial and management resources, some of which would have to be deployed prior to having any certainty of marketing approval.

The Company had cash and cash equivalents of $16.6 million as of December 31, 2018. The Company's existing cash and cash equivalents as of December 31, 2018, will be used primarily to complete the Phase 2b trial of INOpulse for PH-ILD and to complete the dose escalation study for PH-Sarc. As of December 31, 2017, the Company had $2.2 million prepayments of research and development expenses related to its amended drug supply agreement with Ikaria and the clinical research organization it has partnered with for the first of the two Phase 3 clinical trials for INOpulse for PAH. As of December 31, 2018 the prepayments balance was zero.

On October 25, 2016, the Company filed a registration statement on Form S-1 with the SEC, which as amended became effective on November 22, 2016. On November 29, 2016, the Company completed the sale of 17,142,858 Class A Units consisting of an aggregate of 17,142,858 shares of its common stock and warrants exercisable for up to 17,142,858 shares of its common stock at a price of $0.70 per Unit, or the Secondary Offering, resulting in net proceeds of $10.9 million, after deducting placement fees of $0.8 million and offering costs of $0.3 million. Each warrant has an exercise price per full share of common stock equal to $0.80, is immediately exercisable and will expire five years from the date on which such warrant

becomes exercisable. The warrants require cash settlement by the Company under certain situations. During the years ended December 31, 2018 and 2017, the Company received proceeds of $0.2 million for the exercise of 239,824 warrants and $2.3 million for exercise of 2,872,585 warrants, respectively. Refer to Note 6 - Common Stock Warrants for further details on the warrants.

On May 9, 2017, the Company entered into a Securities Purchase Agreement, or the Purchase Agreement, with a single institutional investor for the sale of 2,000,000 shares of its common stock at a purchase price of $1.50 per share and warrants to purchase up to an aggregate of 1,000,000 shares of its common stock, or the Direct Offering. The warrants became exercisable commencing six months from the issuance date at an exercise price equal to $1.50 per full share of common stock, subject to adjustments as provided under the terms of the warrants. The warrants are exercisable for five years from the initial exercise date. In addition, the Company issued to the placement agent of the Direct Offering warrants to purchase up to 60,000 shares. The placement agent warrants have substantially the same terms as the warrants issued to the investor, except that the placement agent warrants have an exercise price equal to $1.875 and will be exercisable for five years from the date of the closing of this offering. The closing of the sales of these securities under the Purchase Agreement occurred on May 15, 2017. The aggregate gross and net proceeds for the Direct Offering were $3.0 million and $2.7 million, respectively.

On September 26, 2017, the Company entered into a Securities Purchase Agreement, or the PIPE Purchase Agreement, pursuant to which the Company sold an aggregate of 19,449,834 shares of its common stock at a purchase price of $1.205 per share and warrants to purchase up to an aggregate of 19,449,834 shares of its common stock, or the PIPE Offering. The warrants will be initially exercisable commencing six months from the issuance date at an exercise price equal to $1.2420 per full share of common stock, subject to adjustments as provided under the terms of the warrants. The warrants are exercisable for five years from the initial exercise date. The closing of the sales of these securities under the PIPE Purchase Agreement occurred on September 29, 2017. The aggregate gross and net proceeds for the PIPE Offering were $23.4 million and $22.8 million, respectively.

On June 25, 2018, the Company filed a shelf registration statement on Form S-3 with the SEC, which became effective on July 6, 2018. The shelf registration allows the Company to issue, from time to time at prices and on terms to be determined prior to the time of any such offering, up to $100 million of any combination of common stock, preferred stock, debt securities, warrants and rights, either individually or in units.

On January 25, 2019, the Company completed the sale of 10,000,000 shares of its common stock at a public offering price of $0.70 per share, resulting in net proceeds of $6.2 million, after deducting placement fees of $0.5 million and offering costs of $0.3 million. The Company also granted the underwriter a 45-day option to purchase up to an additional 1,500,000 shares of its common stock at the public offering price per share, less underwriting discounts and commissions.

The Company continues to pursue potential sources of funding, including equity financing.

The Company evaluated whether there are any conditions and events, considered in the aggregate, that raise substantial doubt about its ability to continue as a going concern within one year beyond the filing of this Annual Report on Form 10-K.

Based on such evaluation, the Company believes that its existing cash and cash equivalents as of December 31, 2018, the proceeds from the January 2019 public offering and proceeds that will become available upon sale of its state net operating losses, or NOLs, and R&D tax credits under the State of New Jersey's Technology Business Tax Certificate Transfer Program will be sufficient to satisfy its operating cash needs for at least one year after the filing of this Annual Report on Form 10-K.

The Technology Business Tax Certificate Transfer Program enables qualified, unprofitable New Jersey based technology or biotechnology companies to sell a percentage of NOL and research and development (R&D) tax credits to unrelated profitable corporations, subject to meeting certain eligibility criteria. Based on consideration of various factors, including application processing time and past trend of benefits made available under the program, the Company believes that it is probable that its plans to sell its NOLs can be effectively implemented to address its short term financial needs. The Company has sold $61.5 million of state NOLs and $0.2 million of Research and Development credits under the State of New Jersey's Technology Business Tax Certificate Transfer Program in February 2018 for net proceeds of $5.3 million and has sold an additional $20.0 million of state NOLs for net proceeds of $1.7 million in January 2019. Subject to state approval and program availability, the Company plans to sell additional NOLs and credits under the same program later in 2019. The proceeds from such sales are recorded as Income tax benefit when sales occur or proceeds are received.

The Company has based its estimates on assumptions that may prove to be wrong, and the Company may exhaust its capital resources sooner than it expects. In addition, the process of testing product candidates in clinical trials is costly, and the timing of progress in clinical trials is uncertain. Because the Company's product candidates are in clinical development and the outcome of these efforts is uncertain, it may not be able to accurately estimate the actual amounts that will be necessary to successfully complete the development and commercialization of its product candidates or whether, or when, it may achieve profitability.

Until such time, if ever, as the Company can generate substantial product revenues, its expects to finance its cash needs through a combination of equity and debt offerings, sales of state NOLs and R&D credits subject to program availability and approval, existing working capital and funding from potential future collaboration arrangements. To the extent that the Company raises additional capital through the future sale of equity or debt, the ownership interest of its existing stockholders will be diluted, and the terms of such securities may include liquidation or other preferences or rights such as anti-dilution rights that adversely affect the rights of its existing stockholders. If the Company raises additional funds through strategic partnerships in the future, it may have to relinquish valuable rights to its technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to it. If the Company is unable to raise additional funds through equity or debt financings when needed, or unable to sell its state NOLs and R&D credits, it may be required to delay, limit, reduce or terminate its product development or future commercialization efforts or grant rights to develop and market product candidates that it would otherwise prefer to develop and market itself. In addition, the timing of when existing and new capital resources are used and received may not align with the period of time evaluated by management for going concern purposes such that management may be required to conclude that substantial doubt about the Company’s ability to continue as a going concern in accordance with relevant accounting guidance may exist in future periods.

(4) Marketable Debt Securities

Marketable securities as of December 31, 2017 consisted of the following (in thousands):

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
US Government bonds	3,000	—	(4)	2,996
Total	3,000	—	(4)	2,996

Maturities of marketable securities classified as available-for-sale were as follows at December 31, 2017 (in thousands):

	December 31, 2017	
	Amortized Cost	Fair Value
Due within one year	3,000	2,996
	3,000	2,996

(5) Property and Equipment

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

	December 31, 2018	December 31, 2017
Machinery and equipment	$ 2,048	$ 2,048
Leasehold improvements	204	204
Furniture and fixtures	276	276
Property and equipment, gross	2,528	2,528
Less accumulated depreciation	(1,864)	(1,502)
	$ 664	$ 1,026

(6) Common Stock Warrants

On November 29, 2016, the Company issued 17,142,858 warrants that were immediately exercisable and will expire 5 years from issuance at an exercise price of $0.80 per share. As the warrants, under certain situations, could require cash settlement, the warrants were classified as liabilities and are recorded at estimated fair value using a Black-Scholes-Merton pricing model. As of December 31, 2018, 13,741,180 of these warrants were outstanding.

On May 15, 2017, the Company issued to an investor warrants to purchase 1,000,000 shares that became exercisable commencing six months from their issuance and will expire five years from the initial exercise date at an exercise price of $1.50 per share. In addition, the Company issued to the placement agent warrants to purchase 60,000 shares that were immediately exercisable and will expire five years from issuance at an exercise price of $1.875 per share. As the warrants, under certain situations, could require cash settlement, the warrants were classified as liabilities and recorded at estimated fair value using a Black-Scholes-Merton pricing model. As of December 31, 2018, all of these warrants were outstanding.

On September 29, 2017, the Company issued warrants to purchase 19,449,834 shares that became exercisable commencing six months from their issuance and will expire five years from the initial exercise date at an exercise price of $1.2420 per share. As the warrants could not require cash settlement, the warrants were classified as equity. As of December 31, 2018, all of these warrants were outstanding.

The following table summarizes warrant activity for the year ended December 31, 2018 (fair value amount in thousands):

	Equity Classified	Liability Classified	
	Warrants	Warrants	Estimated Fair Value
Beginning balance	19,449,834	15,041,004	$ 32,325
Exercises	—	(239,824)	(483)
Change in fair value of common stock warrant liability recognized in consolidated statement of operations	—	—	(24,877)
Ending balance	19,449,834	14,801,180	$ 6,965

The following table summarizes warrant activity for the year ended December 31, 2017 (fair value amount in thousands):

	Equity Classified	Liability Classified	
	Warrants	Warrants	Estimated Fair Value
Beginning balance	—	17,142,858	$ 5,215
Exercises	—	(3,161,854)	(4,411)
Additions	19,449,834	1,060,000	1,118
Change in fair value of common stock warrant liability recognized in consolidated statement of operations	—	—	30,403
Ending Balance	19,449,834	15,041,004	$ 32,325

See Note 7 for determination of fair value of common stock warrant liability.

(7) Fair Value Measurements

Assets and liabilities recorded at fair value on the balance sheets are categorized based upon the level of judgment associated with the inputs used to measure the fair value. Level inputs are as follows:

- Level 1 - Values are based on unadjusted quoted prices for identical assets or liabilities in an active market which the company has the ability to access at the measurement date.
- Level 2 - Values are based on quoted market prices in markets where trading occurs infrequently or whose values are based on quoted prices of instruments with similar attributes in active markets.
- Level 3 - Values are based on prices or valuation techniques that require inputs that are both unobservable and significant to the overall fair value measurement. These inputs reflect management's own assumptions about the assumptions a market participant would use in pricing the asset.

The following table summarizes fair value measurements by level at December 31, 2018 for financial instruments measured at fair value on a recurring basis (in thousands):

(Dollar amounts in thousands)	Level 1	Level 2	Level 3	Total
Common stock warrant liability	$ —	$ —	$ 6,965	$ 6,965

The following table summarizes fair value measurements by level at December 31, 2017 for financial instruments measured at fair value on a recurring basis (in thousands):

(Dollar amounts in thousands)	Level 1	Level 2	Level 3	Total
Marketable securities	$ —	$ 2,996	$ —	$ 2,996
Common stock warrant liability	$ —	$ —	$ 32,325	$ 32,325

The Company uses a Black-Scholes-Merton option pricing model to value its common stock warrants. The significant unobservable inputs used in calculating the fair value of common stock warrants represent management's best estimates and involve inherent uncertainties and the application of management's judgment. For volatility, the Company uses its own historical volatility as well as comparable public companies as a basis for its expected volatility to calculate the fair value of common stock warrants due to its limited history as a public company. The risk-free interest rate is based on U.S. Treasury notes with a term approximating the expected term of the common stock warrant. Any significant increases or decreases in the unobservable inputs, with the exception of the risk-free interest rate, may result in significantly higher or lower fair value measurements.

The following are the weighted average assumptions used in estimating the fair value of warrants outstanding as of December 31, 2018 and 2017:

	December 31, 2018	December 31, 2017
Valuation assumptions:		
Risk-free interest rate	2.45%	2.08%
Expected volatility	93.61%	96.24%
Expected term (in years)	3.0	4.0
Dividend yield	—%	—%

(8) Stock-Based Compensation

Determining the appropriate fair value of stock-based awards requires the input of subjective assumptions, the expected term of the option and expected volatility. The Company uses the Black-Scholes-Merton option pricing model to value its stock option awards. The assumptions used in calculating the fair value of stock-based awards represent management's best estimates and involve inherent uncertainties and the application of management's judgment. The expected term of stock options is estimated using the "simplified method," as the Company has no historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior for its stock options grants. The simplified method is based on the average of the vesting tranches and the contractual life of each grant. For volatility, the Company uses comparable public companies as a basis for its expected volatility to calculate the fair value of option grants due to its limited history as a public company. The risk-free interest rate is based on U.S. Treasury notes with a term approximating the expected term of the option. For restricted stock, the fair value is the closing market price per share on the grant date. The estimation of the number of stock awards that will ultimately vest requires judgment, and to the extent actual results or revised

estimates differ from the Company's current estimates, such amounts will be recorded as an adjustment in the period in which estimates are revised.

Incentive Plans

During 2014, the Company adopted the 2014 Equity Incentive Plan, or the 2014 Plan, which provided for the grant of options. Following the effectiveness of the Company's registration statement filed in connection with its IPO, no options may be granted under the 2014 plan. The awards granted under the 2014 Plan generally have a vesting period of between one to four years.

During 2015, the Company adopted the 2015 Equity Incentive Plan, or the 2015 Plan, which provides for the grant of options, restricted stock and other forms of equity compensation. On May 4, 2017, the Company's stockholders approved an amendment to the 2015 Plan to increase the aggregate number of shares available for the grant of awards to 5,000,000 and to increase the maximum number of shares available under the annual increase to 3,000,000 shares. As of December 31, 2018, the Company had 891 shares available for grant.

As of December 31, 2018, there was approximately $3.7 million of total unrecognized compensation expense related to unvested stock awards. This expense is expected to be recognized over a weighted-average period of 2.5 years.

No tax benefit was recognized during the years ended December 31, 2018, 2017 and 2016 related to stock-based compensation expense since the Company incurred operating losses and has established a full valuation allowance to offset all the potential tax benefits associated with its deferred tax assets.

Options

Compensation expense is measured based on the fair value of the option on the grant date and is recognized on a straight-line basis over the requisite service period, or sooner if vesting occurs sooner than on a straight-line basis. Options are forfeited if the employee ceases to be employed by the Company prior to vesting.

The weighted average grant-date fair value of options issued during the years ended December 31, 2018, 2017 and 2016 was $1.02, $1.05 and $0.52, respectively. The following are the weighted average assumptions used in estimating the fair value of options issued during the years ended December 31, 2018, 2017 and 2016.

	Year Ended		
	December 31, 2018	**December 31, 2017**	**December 31, 2016**
Valuation assumptions:			
Risk-free interest rate	2.74%	2.04%	1.90%
Expected volatility	84.55%	91.02%	82.48%
Expected term (in years)	6.0	6.0	6.2
Dividend yield	—%	—%	—%

A summary of option activity under the 2015 Plan and 2014 Plan for the years ended December 31, 2018, 2017 and 2016 is presented below:

	Bellerophon 2015 and 2014 Equity Incentive Plans			
	Shares	Exercise Price	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life (in years)
Options outstanding as of December 31, 2015	705,180	$ 4.12 - 13.28	$ 12.08	8.7
Granted	2,530,770	0.49 - 2.30	0.73	
Forfeited	(46,069)	10.22 - 13.28	11.69	
Options outstanding as of December 31, 2016	3,189,881	$ 0.49 - 13.28	$ 3.08	9.4
Granted	106,300	1.12 - 2.25	1.39	
Exercised	(1,000)	0.49	0.49	
Forfeited	(25,298)	0.49 - 12.00	1.71	
Options outstanding as of December 31, 2017	3,269,883	$ 0.49 - 13.28	$ 3.04	8.4
Granted	3,683,228	0.91 - 2.92	1.39	
Exercised	(5,875)	0.49 - 1.94	0.52	
Expired	(7,983)	13.28	13.28	
Forfeited	(170,021)	0.49 - 12.00	1.99	
Options outstanding as of December 31, 2018	6,769,232	$ 0.49 - 13.28	$ 2.16	8.6
Options vested and exercisable as of December 31, 2018	1,891,010	$ 0.49 - 13.28	$ 4.51	7.2

The intrinsic value of options outstanding, vested and exercisable as of December 31, 2018 was $0.3 million.

Restricted Stock

The restricted stock awards granted generally have a vesting period of less than one year.

A summary of restricted stock activity under the 2015 Plan for the years ended years ended December 31, 2018, 2017 and 2016 is presented below:

	Bellerophon 2015 Equity Incentive Plan			
	Shares	Weighted Average Fair Value	Aggregate Grant Date Fair Value (in millions)	Weighted Average Remaining Contractual Life (in years)
Restricted stock outstanding as of December 31, 2015	77,793	3.99	$ 0.3	0.7
Granted	519,871	2.40	1.2	
Vested	(417,817)	(2.75)	(1.2)	
Forfeited	(24,001)	(3.69)	(0.1)	
Restricted stock outstanding as of December 31, 2016	155,846	2.05	$ 0.3	0.0
Granted	873,310	1.45	1.3	
Vested	(700,626)	(1.60)	(1.1)	
Restricted stock outstanding as of December 31, 2017	328,530	1.42	$ 0.5	0.2
Granted	1,245,171	1.41	1.8	
Vested	(608,083)	(1.70)	(1)	
Restricted stock outstanding as of December 31, 2018	965,618	1.23	$ 1.2	0.3

Ikaria Equity Incentive Plans for Periods Prior to February 12, 2014

Options

The Company has outstanding options that were assumed during its spin-out from Ikaria, Inc., or Ikaria. A summary of option activity under the assumed Ikaria 2007 stock option plan and the assumed Ikaria 2010 long term incentive plan for the years ended December 31, 2018, 2017 and 2016 is presented below:

	Ikaria Equity Incentive Plans for Periods Prior to February 12, 2014			
	Shares	Range of Exercise Price	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life (in years)
Options outstanding, vested and exercisable as of December 31, 2015	113,709	$ 0.26 - 17.92	$ 8.93	5.2
Forfeited	(26,340)	0.26 - 17.92	8.23	
Options outstanding, vested and exercisable as of December 31, 2016	87,369	$ 7.77 - 17.92	$ 9.14	4.3
Forfeited	(15,160)	7.77 - 14.91	8.81	
Options outstanding, vested and exercisable as of December 31, 2017	72,209	$ 7.77 - 17.92	$ 9.21	4.0
Forfeited	(2,590)	11.65	11.65	
Options outstanding, vested and exercisable as of December 31, 2018	69,619	$ 7.77 - 17.92	$ 9.12	3.2

There were no options exercised during the years ended December 31, 2018, 2017 and 2016. The intrinsic value of options outstanding, vested and exercisable as of December 31, 2018 was zero.

Stock-Based Compensation Expense, Net of Estimated Forfeitures

The following table summarizes the stock-based compensation expense for the years ended December 31, 2018, 2017 and 2016. The following disclosures include stock-based compensation expense recognized under the 2015 Plan and the 2014 Plan (in thousands):

	Year Ended December 31,		
(in thousands)	2018	2017	2016
Research and development	$ 721	$ 850	$ 689
General and administrative	2,234	1,991	2,069
Total expense	$ 2,955	$ 2,841	$ 2,758

(9) Income Taxes

Prior to its conversion to a Delaware corporation in February 2015, the Company was a Delaware limited liability company, or LLC, that passed through income and losses to its members for U.S. federal and state income tax purposes. As a result of its conversion to a Delaware corporation, the Company recognized deferred income taxes through income tax expense related to temporary differences that existed as of the date of its tax status change.

The Company's tax rate for 2018 is (193.2%) due to the fact that it sold its New Jersey state Net Operating Losses and Credits and recognized the sale as a benefit in 2018. The Company expects to generate additional losses and currently has a full valuation allowance. The Company's tax rate for 2017 is 0% because the Company had a full valuation allowance.

On December 22, 2017, the Tax Cuts and Jobs Act (H.R. 1), or the Tax Act, was signed into law. The Tax Act contains significant changes to corporate taxation, including (i) the reduction of the corporate income tax rate to 21%, (ii) the

acceleration of expensing for certain business assets, (iii) the one-time transition tax related to the transition of U.S. international tax from a worldwide tax system to a territorial tax system, (iv) the repeal of the domestic production deduction, (v) additional limitations on the deductibility of interest expense, and (vi) expanded limitations on executive compensation.

The key impact of the Tax Act on our financial statement for the year ended December 31, 2017, was the re-measurement of deferred tax balances to the new corporate tax rate. Due to the fact that the company maintains a full valuation allowance on its deferred tax assets, there was no impact to the balance sheet or statements of operations for this re-measurement.

The Company may be subject to certain limitations in its annual utilization of NOL carry forwards to off-set future taxable income (and of tax credit carry forwards to off-set future tax expense) pursuant to Section 382 of the Internal Revenue Code, which could result in tax attributes expiring unused.

A reconciliation of the statutory federal income tax rate to the Company's effective tax rate for the years ended December 31, 2018, 2017 and 2016 is as follows:

	Year Ended December 31, 2018	Year Ended December 31, 2017	Year Ended December 31, 2016
U.S. federal statutory rate	21 %	34 %	34 %
2017 Tax Act	— %	(23.9)%	— %
State and local taxes, net of federal tax effect	105.9 %	5.7 %	6.6 %
Research tax credits	(53.3)%	10.4 %	13.7 %
Valuation allowance	104 %	(4.5)%	(38.9)%
Prior year adjustments	5.4 %	0.9 %	(13.7)%
Sale of R&D tax credits	(193.3)%	— %	(1.8)%
Expenses associated with common stock warrant liability (a)	(185.6)%	(18.9)%	(1.3)%
Incentive stock options, non-deductible	2.7 %	(3.8)%	(0.4)%
	(193.2)%	0 %	(1.8)%

(a) Represents change in fair value and attributable issuance costs

Deferred taxes as of December 31, 2018 and 2017 reflect the tax effects of the differences between the amounts recorded as assets and liabilities for financial reporting purposes and the comparable amounts recorded for income tax purposes.

Significant components of the deferred tax assets (liabilities) at December 31, 2018 are as follows (in thousands):

	December 31, 2018	
	Assets	(Liabilities)
Net operating loss carryforwards	$ 22,325	$ —
Research tax credit carryforwards	23,828	—
Property and equipment	—	(69)
Stock based compensation	1,290	—
Intangible assets	6,691	—
Accrued expenses	920	—
Subtotal	55,054	(69)
Valuation allowance	(54,985)	—
Total deferred tax assets (liabilities)	$ 69	$ (69)
Net deferred tax assets	$ —	

Significant components of the deferred tax assets (liabilities) at December 31, 2017 are as follows (in thousands):

	December 31, 2017	
	Assets	(Liabilities)
Net operating loss carryforwards	$ 21,006	$ —
Research tax credit carryforwards	22,246	—
Property and equipment	—	(89)
Stock based compensation	980	—
Intangible assets	7,354	—
Accrued expenses	562	—
Subtotal	52,148	(89)
Valuation allowance	(52,059)	—
Total deferred tax assets (liabilities)	$ 89	$ (89)
Net deferred tax assets	$ —	

A valuation allowance is provided when it is more likely than not that some portion or all of the deferred tax assets will not be realized. As of December 31, 2018, management believed that it was more likely than not that the deferred tax assets would not be realized, based on future operations, consideration of tax strategies and the reversal of deferred tax liabilities. The valuation allowance is required until the Company has sufficient positive evidence of taxable income necessary to support realization of its deferred tax assets. A valuation allowance release is recognized as an income tax benefit.

As of December 31, 2018, the Company has available net operating loss, or NOL, carry forwards for federal income tax reporting purposes of approximately $89.1 million and for state income tax reporting purposes of approximately $50.7 million, which expire at various dates between fiscal 2034 and 2038. In February 2018, the Company sold $61.5 million of state NOLs and $0.2 million of R&D credits from 2015 and 2016 under the State of New Jersey's Technology Business Tax Certificate Transfer Program. In January 2019, the Company sold $20.0 million of state NOLs from 2017 under the same program and plans to sell additional NOLs and R&D credits under the same program in the future subject to program availability and state approval. As of December 31, 2017 and 2016, the Company had no material uncertain tax positions.

(10) Net Income (Loss) Per Share

	Twelve months ended December 31,		
	2018	2017	2016
Net income (loss)	$ 2,814	$ (54,818)	$ (23,814)
Weighted-average shares:			
Basic	57,446,537	38,950,937	15,057,627
Effect of dilutive securities:			
Warrants	7,602,355	—	—
Diluted	65,048,892	38,950,937	15,057,627
Net income (loss) per share:			
Basic	$ 0.05	$ (1.41)	$ (1.58)
Diluted	$ (0.34)	$ (1.41)	$ (1.58)

For the year ended December 31, 2018, the total number of potential shares of common stock excluded from the diluted earnings per share computation because their inclusion would have been anti-dilutive was 34.4 million which included 6.8 million options to purchase shares, 1.0 million restricted shares and 26.6 million warrants to purchase shares.

As of December 31, 2017, the Company had 34,780,107 common stock warrants, 3,342,092 options to purchase shares and 328,530 restricted shares outstanding that have been excluded from the computation of diluted weighted average shares outstanding, because such securities had an antidilutive impact due to the loss reported. As of December 31, 2016, the Company had 17,142,858 common stock warrants, 3,277,250 options to purchase shares and 155,846 restricted shares outstanding that have been excluded from the computation of diluted weighted average units outstanding, because such securities had an antidilutive impact due to the loss reported.

Basic net income (loss) per share is calculated by dividing net income (loss) by the weighted average number of shares outstanding during the period, as applicable. Diluted net loss per share is calculated by dividing net income (loss), adjusted to reflect the impact of dilutive warrants, by the weighted average number of shares outstanding, adjusted to reflect potentially dilutive securities using the treasury stock method, except when the effect would be anti-dilutive.

(11) Commitments and Contingencies

Legal Proceedings

The Company periodically becomes subject to legal proceedings and claims arising in connection with its business. The ultimate legal and financial liability of the Company in respect to all proceedings, claims and lawsuits, pending or threatened, cannot be estimated with any certainty.

As of the date of this report, the Company is not aware of any proceeding, claim or litigation, pending or threatened, that could, individually or in the aggregate, have a material adverse effect on the Company's business, operating results, financial condition and/or liquidity.

Operating Leases

The following is a summary of the Company's long-term contractual cash obligations as of December 31, 2018 (in thousands):

	Operating Lease(1)
2019	$ 653
2020	663
2021	674
2022	686
2023	172
Thereafter	—
Total	$ 2,848

(1) Operating lease obligations include the lease agreement the Company entered into on August 6, 2015 for office space in Warren, New Jersey.

Rent expense is calculated on the straight-line basis and amounted to approximately $0.7 million, $0.7 million, $0.4 million for the years ended December 31, 2018, 2017 and 2016, respectively.

Royalty payments and success-based milestones associated with the Company's license and supply agreements with Ikaria have not been included in the above table of contractual obligations as the Company cannot reasonably estimate if or when they will occur.

License Agreement with Ikaria

In February 2014, the Company entered into a cross-license, technology transfer and regulatory matters agreement with a subsidiary of Ikaria. Pursuant to the terms of the license agreement, Ikaria granted to the Company 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 who have PAH, PH-COPD or PH associated with idiopathic pulmonary fibrosis, or PH-IPF. Pursuant to the terms of the license agreement, the Company granted Ikaria a fully paid-up, non-royalty-bearing, exclusive license under specified intellectual property rights that the Company controls 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 PAH, PH-COPD or PH-IPF and for the use of nitric oxide to treat or prevent conditions that are primarily managed in the hospital. The Company agreed that, during the term of the license agreement, it will not, without the prior written consent of Ikaria, grant a sublicense under any of the intellectual property licensed to the Company under the license agreement to any of its affiliates or any third party, in either case, that directly or indirectly competes with Ikaria's nitric oxide business. In July 2015, the Company and Ikaria entered into an amendment to the license agreement to expand the scope of the Company's license to allow the Company to develop its INOpulse program for the treatment of three additional indications: chronic thromboembolic PH, or 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, the Company entered into an amendment to its 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. In April 2018, we expanded the scope of our license from PH-IPF to PH in patients with Pulmonary Fibrosis (PH-PF), which includes idiopathic interstitial pneumonias, chronic hypersensitivity pneumonitis, occupational and environmental lung disease, with a royalty equal to 1% of net sales of any commercial products for PH-PF.

Agreements Not to Compete

In September 2013, October 2013 and February 2014, the Company entered into an agreement not to compete with 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, the Company 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 as specified in the agreements.

In the course of its normal business operations, the Company also enters into agreements with contract service providers and others to assist in the performance of its research and development and manufacturing activities. The Company can elect to discontinue the work under these contracts and purchase orders at any time with notice, and such contracts and purchase orders do not contain minimum purchase obligations.

In August 2009, the Company entered into a license agreement with BioLineRx Ltd. and BioLine Innovations Jerusalem L.P., which are referred to collectively as BioLine, under which the Company obtained an exclusive worldwide license to BCM. In July 2018, the Company informed BioLineRx Ltd., from whom it in-licensed the BCM technology, on its decision to discontinue further development and terminate the License and Commercialization Agreement.

(12) Quarterly Financial Data (unaudited)

	Three Months Ended December 31,		Three Months Ended September 30,		Three Months Ended June 30,		Three Months Ended March 31,	
(in thousands, except share/ and per share data)	2018	2017	2018	2017	2018	2017	2018	2017
Operating expenses:								
Research and development	$ 2,817	$ 5,390	$ 5,247	$ 4,438	$ 5,815	$ 4,689	$ 6,380	$ 3,337
General and administrative	1,867	1,919	1,584	1,746	2,058	1,634	2,112	1,446
Total operating expenses	4,684	7,309	6,831	6,184	7,873	6,323	8,492	4,783
Loss from operations	(4,684)	(7,309)	(6,831)	(6,184)	(7,873)	(6,323)	(8,492)	(4,783)
Change in fair value of common stock warrant liability	3,676	(16,948)	17,840	(1,435)	(3,689)	2,367	7,050	(14,387)
Interest income	96	98	92	33	91	26	99	27
Pre-tax (loss) income	(912)	(24,159)	11,101	(7,586)	(11,471)	(3,930)	(1,343)	(19,143)
Income tax benefit	—	—	—	—	—	—	5,439	—
Net loss (income)	$ (912)	$ (24,159)	$ 11,101	$ (7,586)	$ (11,471)	$ (3,930)	$ 4,096	$ (19,143)
Weighted average shares outstanding:								
Basic	57,713,874	55,109,847	57,710,251	34,989,831	57,229,459	33,558,669	57,059,686	31,934,253
Diluted	59,575,730	55,109,847	64,544,504	34,989,831	57,229,459	40,491,044	72,100,690	31,934,253
Net income (loss) per share:								
Basic	$ (0.02)	$ (0.44)	$ 0.19	$ (0.22)	$ (0.20)	$ (0.12)	$ 0.07	$ (0.60)
Diluted	$ (0.08)	$ (0.44)	$ (0.10)	$ (0.22)	$ (0.20)	$ (0.15)	$ (0.04)	$ (0.60)

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

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

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

Management's Annual Report on Internal Control Over Financial Reporting

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

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

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

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

Based on our assessment, management believes that, as of December 31, 2018, our internal control over financial reporting is effective based on those criteria**.** Our independent registered public accounting firm has not performed an evaluation of our internal control over financial reporting during any period in accordance with the provisions of the Sarbanes-Oxley Act. For as long as we remain an "emerging growth company" as defined in the JOBS Act, we intend to take advantage of this exemption.

Changes in Internal Control Over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the fiscal quarter ended December 31, 2018 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Directors

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Management and Corporate Governance," "Section 16(a) Beneficial Ownership Reporting Compliance," and "Code of Conduct and Ethics" in our Proxy Statement for the 2019 Annual Meeting of Stockholders (our "2019 Proxy Statement").

On March 12, 2019, based on the Nominating and Corporate Governance Committee's recommendation, the Board of Directors appointed Crispin Teufel as a director effective March 18, 2019. Mr. Teufel will represent Linde North America, Inc. (Linde), our fourth largest shareholder. Jens Luehring, who has recently left Linde to become CEO of a newly formed spin off company, will not stand for reelection at our annual meeting of stockholders and will be succeeded by Mr. Teufel. Additionally, Daniel Tasse has recently assumed new CEO responsibilities that require him to step down from our Board and will also not stand for reelection. Messrs. Tassé and Luehring will continue to serve as members of our board of directors until their terms expire at the conclusion of the 2019 Annual Meeting of Stockholders.

Mr. Crispin Teufel will join as a member of our Audit Committee and Compensation Committee. Mr. Teufel's biography is set forth below. Mr. Teufel will receive compensation for his service as a non-employee director in accordance with the Company's previously disclosed amended director compensation program, including the award of a one-time nonqualified stock option under the Company's 2015 Equity Incentive Plan to purchase 25,000 shares of Common Stock.

Crispin Teufel was appointed to our Board effective March 18, 2019. Since 2017, Mr. Teufel has served as the Chief Executive Officer of Lincare Holdings Inc., the leading national provider of respiratory services in the home, and as its Chief Financial Officer since 2013. Mr. Teufel serves on the board of directors of the German-American Chamber of Commerce. Mr. Teufel holds an MBA in Economics from Ruhr University Bochum, Germany, is a Certified Public Accountant and is a German Tax Advisor under Germany's Taxation and Ministry of Finance. We believe that Mr. Teufel is qualified to serve on our Board because of his managerial, financial and business experience.

Executive Officers

The following table sets forth the name, age and position of each of our executive officers as of March 12, 2019.

Name	Age	Position
Fabian Tenenbaum	45	Chief Executive Officer
Peter Fernandes	64	Chief Regulatory and Safety Officer
Assaf Korner	41	Chief Financial Officer and Secretary
Martin Dekker	46	Vice President of Engineering and Manufacturing
Amy Edmonds	47	Vice President of Clinical Operations and Administration
Parag Shah	42	Vice President of Business Operations

Fabian Tenenbaum has served as our Chief Executive Officer since November 2016. Prior to then Mr. Tenenbaum served as Chief Financial Officer and Chief Business Officer from February 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 October 2014 to February 2016. Prior to that, Mr. Tenenbaum served as Chief Executive Officer with Syneron Beauty from 2011 to October 2014, and Chief Financial Officer and Executive Vice President of Syneron Medical from May 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.

Peter Fernandes has been our Chief Regulatory and Safety Officer since May 2015. 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 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.

Assaf Korner has served as our Chief Financial Officer and Secretary since January 2018. Prior to joining us, Mr. Korner served as the Chief Financial Officer of L&R Distributors, a national distributor, since February 2016. Prior to that, Mr. Korner served as the Chief Financial Officer of Iluminage Beauty, a Joint Venture between Unilever and Syneron Medical, from 2011 through January 2016. Prior to Iluminage Beauty, Mr. Korner held several senior finance roles in Syneron Medical from 2005 through 2011. Prior to Syneron Medical, Mr. Korner served as a Senior Auditor at KPMG. Mr. Korner holds an MBA from Tel-Aviv University, Israel, a Bachelor's degree in Accounting and Economics from Haifa University, Israel and is a Certified Public Accountant.

Martin Dekker has served as our Vice President of Engineering and Manufacturing 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 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 Business Operations since April 2016 with responsibilities for Project Management, Supply Distribution, Pre-Clinical and Business Development activities. Prior to joining us, 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.

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

Code of Ethics and Code of Conduct

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. We have posted a current copy of the code on our website, www.bellerophon.com. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

Section 16(a) Beneficial Ownership Reporting Compliance

The information concerning compliance with Section 16(a) of the Securities Exchange Act of 1934 required by this Item is incorporated by reference to the "Section 16(a) Beneficial Ownership Reporting Compliance" section of our 2019 Proxy Statement.

Item 11. Executive Compensation

The response to this item is incorporated by reference from the discussion responsive thereto under the caption "Executive Officer and Director Compensation" in our 2019 Proxy Statement.

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

The response to this item is incorporated by reference from the discussion responsive thereto under the captions “Security Ownership of Certain Beneficial Owners and Management,” “Equity Compensation Plan Information” and “Increase in the Number of Shares To Be Granted Under the Company's 2015 Equity Plan (Proposal No. 3)” in our 2019 Proxy Statement.

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

The response to this item is incorporated by reference from the discussion responsive thereto under the captions “Certain Relationships and Related Person Transactions” and “Management and Corporate Governance” in our 2019 Proxy Statement.

Item 14. Principal Accountant Fees and Services

The response to this item is incorporated by reference from the discussion responsive thereto under the caption “Independent Registered Public Accounting Firm” in our 2019 Proxy Statement.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(1) Financial Statements

Our consolidated financial statements are set forth in Part II, Item 8 of this Annual Report on Form 10-K and are incorporated herein by reference.

(2) Financial Statement Schedules

No financial statement schedules have been filed as part of this Annual Report on Form 10-K because they are not applicable or are not required or because the information is otherwise included herein.

(3) Exhibits

The exhibits filed as part of this Annual Report on Form 10-K are set forth on the Exhibit Index immediately following our financial statements. The Exhibit Index is incorporated herein by reference.

Item 16. Form 10-K Summary

None.

EXHIBIT INDEX

Exhibit Number	Description of Exhibit
3.1	Restated Certificate of Incorporation of the Registrant, as amended, dated July 30, 2018 (incorporated by reference to Exhibit 3.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-36845) filed with the SEC on November 7, 2018)
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-36845) filed with the SEC on February 25, 2015)
4.1	Specimen Stock Certificate evidencing the shares of common stock (incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1/A (File No. 333-201474) filed with the SEC on February 3, 2015)
4.2	Stockholders Agreement, dated February 12, 2015, between the Registrant and Linde North America, Inc. (incorporated by reference to Exhibit 4.2 to the Registrant's Annual Report on Form 10-K (File No. 001-36845) filed with the SEC on March 31, 2015)
4.3	Stockholders Agreement, dated February 12, 2015, among the Registrant and New Mountain Partners II (AIV-A), L.P., New Mountain Partners II (AIV-B), L.P., New Mountain Affiliated Investors II, L.P. and Allegheny New Mountain Partners, L.P. (incorporated by reference to Exhibit 4.3 to the Registrant's Annual Report on Form 10-K (File No. 001-36845) filed with the SEC on March 31, 2015)
10.1+	Assumed 2007 Ikaria Stock Option Plan (incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-201474) filed with the SEC on January 13, 2015)
10.2+	Assumed 2010 Ikaria Long Term Incentive Plan (incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-201474) filed with the SEC on January 13, 2015)
10.3+	2014 Equity Incentive Plan (incorporated by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form S-1 (File No. 333-201474) filed with the SEC on January 13, 2015)
10.4+	Form of Option Agreement under 2014 Equity Incentive Plan (incorporated by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form S-1 (File No. 333-201474) filed with the SEC on January 13, 2015)
10.5+	Amended and Restated 2015 Equity Incentive Plan (incorporated by reference to Appendix A to the Registrant's Definitive Proxy Statement (File No. 001-36845) filed with the SEC on March 20, 2017)
10.6+	Form of Incentive Stock Option Agreement under 2015 Equity Incentive Plan (incorporated by reference to Exhibit 10.6 to the Registrant's Registration Statement on Form S-1/A (File No. 333-201474) filed with the SEC on February 3, 2015)
10.7+	Form of Nonstatutory Stock Option Agreement under 2015 Equity Incentive Plan (incorporated by reference to Exhibit 10.7 to the Registrant's Registration Statement on Form S-1/A (File No. 333-201474) filed with the SEC on February 3, 2015)
10.8†	Amended and Restated License and Commercialization Agreement, dated as of August 26, 2009, among Ikaria Development Subsidiary One LLC, BioLineRx Ltd. and BioLine Innovations Jerusalem L.P., as amended (incorporated by reference to Exhibit 10.8 to the Registrant's Annual Report on Form 10-K (File No. 001-36845) filed with the SEC on March 31, 2015)
10.9	Form of Agreement Not to Compete, entered into by Ikaria Acquisition LLC and each of the Registrant, Bellerophon BCM LLC, Bellerophon Pulse Technologies LLC and Bellerophon Services, Inc. (incorporated by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S-1 (File No. 333-201474) filed with the SEC on January 13, 2015)
10.10†	Drug Clinical Supply Agreement, dated as of February 9, 2014, between Bellerophon Pulse Technologies LLC and INO Therapeutics LLC (incorporated by reference to Exhibit 10.12 to the Registrant's Registration Statement on Form S-1 (File No. 333-201474) filed with the SEC on January 13, 2015)
10.11†	Exclusive Cross-License, Technology Transfer and Regulatory Matters Agreement, dated February 9, 2014, between Bellerophon Pulse Technologies LLC and INO Therapeutics LLC, as amended on March 27, 2014 (incorporated by reference to Exhibit 10.14 to the Registrant's Registration Statement on Form S-1 (File No. 333-201474) filed with the SEC on January 13, 2015)

10.12	Registration Rights Agreement, dated February 12, 2015, among the Registrant, New Mountain Partners II (AIV-A), L.P., New Mountain Partners II (AIV-B), L.P., Allegheny New Mountain Partners, L.P., New Mountain Affiliated Investors II, L.P., ARCH Venture Fund VI, L.P., Venrock Partners, L.P., Venrock Associates IV, L.P., Venrock Entrepreneurs Fund IV, L.P., Linde North America, Inc., 5AM Ventures LLC and Aravis Venture I L.P. (incorporated by reference to Exhibit 10.16 to the Registrant's Annual Report on Form 10-K (File No. 001-36845) filed with the SEC on March 31, 2015)
10.13	Form of Indemnification Agreement between the Registrant and each of its executive officers and directors (incorporated by reference to Exhibit 10.17 to the Registrant's Registration Statement on Form S-1 (File No. 333-201474) filed with the SEC on January 13, 2015)
10.14+	Employment Agreement, dated June 20, 2014, between Jonathan M. Peacock, the Registrant and Bellerophon Services, Inc. (incorporated by reference to Exhibit 10.22 to the Registrant's Registration Statement on Form S-1 (File No. 333-201474) filed with the SEC on January 13, 2015)
10.15	Form of Management Rights Letter between the Registrant and certain of its stockholders (incorporated by reference to Exhibit 10.23 to the Registrant's Registration Statement on Form S-1 (File No. 333-201474) filed with the SEC on January 13, 2015)
10.16+	Amendment to Assumed Employment Agreement, dated as March 13, 2015, between Jonathan M. Peacock and the Registrant (incorporated by reference to Exhibit 10.9 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-36845) filed with the SEC on May 15, 2015)
10.17+	Offer Letter, dated April 20, 2015, between Peter Fernandes and the Registrant (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-36845) filed with the SEC on August 14, 2015)
10.18+	Offer Letter, dated December 8, 2014, between Martin Dekker and the Registrant (incorporated by reference to Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-36845) filed with the SEC on August 14, 2015)
10.19	Lease Agreement between 184 Property Owner, LLC and the Registrant dated August 6, 2015 (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-36845) filed with the SEC on November 12, 2015)
10.20	Second Amendment to the Exclusive Cross-License, Technology Transfer, and Regulatory Matters Agreement between Bellerophon Pulse Technologies LLC and INO Therapeutics LLC, dated July 27, 2015 (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-36845) filed with the SEC on November 12, 2015)
10.21	Form of Amendment to Agreement Not to Compete, entered into by Ikaria Acquisition LLC and each of the Registrant, Bellerophon BCM LLC, Bellerophon Pulse Technologies LLC and Bellerophon Services, Inc. dated July 27, 2015 (incorporated by reference to Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-36845) filed with the SEC on November 12, 2015)
10.22+	Offer Letter between Deborah Quinn and the Registrant dated December 8, 2014 (incorporated by reference to Exhibit 10.8 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-36845) filed with the SEC on November 12, 2015)
10.23+	Offer Letter between Amy Edmonds and the Registrant dated February 14, 2014 (incorporated by reference to Exhibit 10.9 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-36845) filed with the SEC on November 12, 2015)
10.24+	Form of Restricted Stock Agreement under 2015 Equity Incentive Plan (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-36845) filed with the SEC on December 4, 2015)
10.25	Second Amendment to Drug Clinical Supply Agreement and Third Amendment to Exclusive Cross-License, Technology Transfer, and Regulatory Matters Agreement, dated November 16, 2015, between Bellerophon Pulse Technologies LLC and INO Therapeutics LLC (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-36845) filed with the SEC on January 12, 2016)
10.26+	Employment Agreement between the Registrant and Fabian Tenenbaum, effective as of November 11, 2016 (incorporated by reference to Exhibit 10.1 to the registrant's Current Report on Form 8-K filed with the SEC on November 15, 2016)
10.27+	Amended and Restated Employment Agreement between Jonathan M. Peacock and the Registrant dated March 12, 2016 (incorporated by reference to Exhibit 10.44 to the Registrant's Annual Report on Form 10-K (File No. 001-36845) filed with the SEC on March 21, 2016)
10.28	Form of Securities Purchase Agreement (incorporated by reference to Exhibit 10.46 to the Registrant's Registration Statement on Form S-1/A (File No. 333-214230) filed with the SEC on November 21, 2016)
10.29	Form of Securities Purchase Agreement, dated May 9, 2017, by and between Bellerophon Therapeutics, Inc. and the purchaser named therein (incorporated by reference to Exhibit 10.1 on Form 8-K filed with the SEC on May 11, 2017)
10.30	Engagement Letter between Bellerophon Therapeutics, Inc. and H.C. Wainwright & Co., LLC, dated as of May 9, 2017 (incorporated by reference to Exhibit 10.2 on Form 8-K filed with the SEC on May 11, 2017)

10.31	Securities Purchase Agreement, dated September 26, 2017, among the Registrant and the investors named therein (incorporated by reference to Exhibit 10.1 on Form 8-K filed with the SEC on September 27, 2017)
10.32	Registration Rights Agreement, dated September 26, 2017, among the Registrant and the investors named therein (incorporated by reference to Exhibit 10.2 on Form 8-K filed with the SEC on September 27, 2017)
10.33+	Offer Letter between Assaf Korner and the Registrant dated December 18, 2017 (incorporated by reference to Exhibit 5.02 on Form 8-K filed with the SEC on December 20, 2017)
10.34+	Form of Retention Agreement by and between the Registrant and each of all Company's employees (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-36845) filed with the SEC on August 13, 2018)
21.1	Subsidiaries of the Registrant (incorporated by reference to Exhibit 21.1 to the Registrant's Registration Statement on Form S-1 (File No. 333-201474) filed with the SEC on January 13, 2015)
23.1	Consent of KPMG LLP independent registered public accounting firm
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended
32	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

* Schedules and exhibits have been omitted pursuant to Item 601(b)(2) of Regulation S-K. The Registrant hereby undertakes to furnish copies of any of the omitted schedules and exhibits upon request by the Securities and Exchange Commission.

† Confidential treatment has been granted as to certain portions, which portions have been omitted and separately filed with the Securities and Exchange Commission.

\+ Management contract or compensatory plan or arrangement filed in response to Item 15(a)(3) of the Instructions to the Annual Report on Form 10-K.

SIGNATURES

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

Date: March 14, 2019

BELLEROPHON THERAPEUTICS, INC.

By: /s/ Fabian Tenenbaum
Fabian Tenenbaum
Chief Executive Officer

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

Signature	Title	Date
/s/ Fabian Tenenbaum Fabian Tenenbaum	Chief Executive Officer and Director (Principal Executive Officer)	March 14, 2019
/s/ Assaf Korner Assaf Korner	Chief Financial Officer and Secretary (Principal Financial Officer and Principal Accounting Officer)	March 14, 2019
/s/ Jonathan M. Peacock Jonathan M. Peacock	Chairman	March 14, 2019
/s/ Naseem Amin Naseem Amin	Director	March 14, 2019
/s/ Scott P. Bruder Scott P. Bruder	Director	March 14, 2019
/s/ Mary Ann Cloyd Mary Ann Cloyd	Director	March 14, 2019
/s/ Jens Luehring Jens Luehring	Director	March 14, 2019
/s/ Andre V. Moura Andre V. Moura	Director	March 14, 2019
/s/ Daniel Tassé Daniel Tassé	Director	March 14, 2019
/s/ Matthew M. Bennett Matthew M. Bennett	Director	March 14, 2019
/s/ Ted Wang Ted Wang	Director	March 14, 2019

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

The Board of Directors
Bellerophon Therapeutics, Inc.:

We consent to the incorporation by reference in the registration statements (Nos. 333-219387, 333-210312, 333-202069 and 333-225871) on Form S-8, the registration statements (Nos. 333-221087, 333-211166 and 333-225878) on Form S-3 and the registration statement (Nos. 333-214773 and 333-214230) on Form S-1 of Bellerophon Therapeutics, Inc. of our report dated March 14, 2019, with respect to the consolidated balance sheets of Bellerophon Therapeutics, Inc. as of December 31, 2018 and 2017, and the related consolidated statements of operations, comprehensive income (loss), changes in stockholders' equity (deficiency in assets), and cash flows for each of the years in the three-year period ended December 31, 2018, and the related notes (collectively, the "consolidated financial statements"), which report appears in the December 31, 2018 annual report on Form 10-K of Bellerophon Therapeutics, Inc.

/s/ KPMG LLP
Short Hills, New Jersey
March 14, 2019

Exhibit 31.1

CERTIFICATION

I, Fabian Tenenbaum, certify that:

1. I have reviewed this Annual Report on Form 10-K of Bellerophon Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 14, 2019

By: /s/ Fabian Tenenbuam

Fabian Tenenbaum
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION

I, Assaf Korner, certify that:

1. I have reviewed this Annual Report on Form 10-K of Bellerophon Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 14, 2019

By: /s/ Assaf Korner

Assaf Korner
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (subsections (a) and (b) of Section 1350, Chapter 63 of Title 18, United States Code), each of the undersigned officers of Bellerophon Therapeutics, Inc., a Delaware corporation (the "Company"), does hereby certify, to such officer's knowledge, that:

(1) the Company's Annual Report on Form 10-K for the year ended December 31, 2018 (the "Report") fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 14, 2019

By: /s/ Fabian Tenenbaum

Fabian Tenenbaum
Chief Executive Officer
(Principal Executive Officer)

Date: March 14, 2019

By: /s/ Assaf Korner

Assaf Korner
Chief Financial Officer
(Principal Financial Officer)