

Bellerophon Therapeutics, Inc.
Form 424B5
January 23, 2019

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-225878

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been declared effective by the Securities and Exchange Commission. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and we are not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to Completion, dated January 22, 2019

PRELIMINARY PROSPECTUS SUPPLEMENT
(TO PROSPECTUS DATED JULY 6, 2018)

Shares

Common Stock

We are offering shares of our common stock. Our common stock is listed on the Nasdaq Global Market under the symbol "BLPH." On January 22, 2019, the last reported sale price of our common stock as reported on the Nasdaq Global Market was \$0.88 per share.

Investing in our common stock involves a high degree of risk. You should read carefully this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein before you invest. See "Risk Factors" beginning on page S-7 of this prospectus supplement and page 7 of the accompanying prospectus.

We are an emerging growth company as that term is used in the Jumpstart Our Business Startups Act of 2012 and, as such, have elected to rely on certain reduced public company disclosure requirements.

| | Per Share | Total |
|--|--------------|-------|
| Public Offering Price | \$ | \$ |
| Underwriting discounts and commissions (1) | \$ | \$ |
| Proceeds, before expenses, to us | \$ | \$ |

(1) We have agreed to reimburse the underwriter for certain expenses. See "Underwriting."

We have granted the underwriter an option for a period of 45 days from the date of this prospectus supplement to purchase up to an additional shares of common stock at the public offering price less underwriting discounts and commissions. If the underwriter exercises the option in full, the total underwriting discounts and commissions payable by us will be \$ and the total proceeds to us, before expenses, will be \$.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of anyone's investment in these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The underwriter expects to deliver the shares of common stock to purchasers on or about , 2019.

H.C. Wainwright & Co.

The date of this prospectus supplement is , 2019.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein. The second part, the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date-for example, a document incorporated by reference in the accompanying prospectus-the statement in the document having the later date modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

We have not and H.C. Wainwright & Co., LLC has not authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus supplement, in the accompanying prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We and H.C. Wainwright & Co., LLC take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you.

This prospectus supplement and the accompanying prospectus do not constitute an offer to sell, or a solicitation of an offer to purchase, the securities offered by this prospectus supplement and the accompanying prospectus in any jurisdiction to or from any person to whom or from whom it is unlawful to make such offer or solicitation of an offer in such jurisdiction. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and in any free writing prospectus that we have authorized for use in connection with this offering is accurate only as of the date of those respective documents. It is important for you to read and consider all information contained in this prospectus supplement and in the accompanying prospectus, including the documents incorporated by reference herein and therein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you in the sections entitled "Where You Can Find More Information" and "Incorporation by Reference" in this prospectus supplement and in the accompanying prospectus.

Other than in the United States, no action has been taken by us or H.C. Wainwright & Co., LLC that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

Unless the context otherwise indicates, references in this prospectus to "we," "our" and "us" refer, collectively, to Bellerophon Therapeutics, Inc., a Delaware corporation, and its consolidated subsidiaries.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein include "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "might," "plan," "predict," "project," "target," "potential," "goals," "will," "would," "could," "should," "continue" and 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 prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein 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;

our ability to continue as a going concern within one year beyond the filing of our Quarterly Report on Form 10-Q for the quarter ended September 30, 2018;

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 expectations related to the use of proceeds from this offering;

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 prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein, particularly in the "Risk Factors" sections of these documents 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.

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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.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information contained elsewhere in this prospectus supplement and the accompanying prospectus and in the documents incorporated by reference herein and therein. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, especially the risks of investing in our common stock discussed under "Risk Factors" beginning on page S-7 of this prospectus supplement and in the documents incorporated by reference herein, along with our financial statements and notes to those financial statements and the other information incorporated by reference in this prospectus supplement and the accompanying prospectus.

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.

Our Development Program

The following table summarizes key information about INOpulse and indications for which we have worldwide commercialization rights.

From the inception of our business through September 30, 2018, \$279.2 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 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 blood circulation, 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-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. 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-IPF. 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.

Wearable medical-grade activity monitoring (Actigraphy) is designed to provide continuous objective real-world physical activity data and is scientifically validated to assess patient outcomes. 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.

INOpulse for PH-COPD

We are also developing INOpulse for the treatment of pulmonary hypertension associated with chronic obstructive pulmonary disease (PH-COPD). Chronic obstructive pulmonary disease (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 long term oxygen therapy (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

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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 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 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 study 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 statistically significant and clinically meaningful increase in 6 minute walk distance (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 we reached agreement with the FDA on all key aspects of our planned Phase 2b study of INOpulse for treatment of PH-COPD.

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 which 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 in 2019.

INOpulse for PAH

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 study, and a second confirmatory randomized withdrawal study with approximately 40 patients who will be crossing over from the INOvation-1 study, can serve as the two adequate and well-controlled studies 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 improvement in pulmonary vascular resistance, cardiac output and NT Pro-BNP (a peptide marker for right ventricular function), however, the DMC deemed 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 6 minute walk distance was improved when subjects were on less background therapies and more patients declined in 6MWD on placebo as compared to iNO. In addition, INOpulse was well tolerated and there were no safety concerns.

Corporate Information

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

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

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Implications of Being an Emerging Growth Company

As a company with less than \$1.07 billion of revenue during our last fiscal year, we qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, and we may remain an emerging growth company until December 31, 2020, subject to the satisfaction of certain conditions. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure and other requirements that are applicable to other public companies that are not emerging growth companies. In particular, in this prospectus supplement and the accompany prospectus, we have not included all of the executive compensation related information that would be required if we were not an emerging growth company. Accordingly, the information contained or incorporated by reference herein may be different than the information you receive from other public companies in which you hold stock.

THE OFFERING

| | |
|--|--|
| Common stock offered by us | Shares |
| Common stock to be outstanding immediately following this offering | Shares |
| Underwriter's option to purchase additional shares | We have granted the underwriter an option for a period of 45 days to purchase up to additional shares of our common stock. |
| Use of proceeds | We estimate that the net proceeds to us from this offering, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately \$ million, or \$ million if the underwriter exercises its option to purchase additional shares in full. We currently estimate that we will use the net proceeds from this offering, together with our existing cash and cash equivalents, for working capital and other general corporate purposes and pursuit of our other research and development efforts. See the "Use of Proceeds" section in this prospectus supplement for more information. |
| Risk Factors | You should read the "Risk Factors" section of this prospectus supplement, as well as those risk factors that are incorporated by reference in this prospectus supplement and the accompanying prospectus, for a discussion of factors to consider carefully before deciding to invest in shares of our common stock. |
| Nasdaq Global Market symbol | "BLPH" |

The number of shares of our common stock to be outstanding after this offering is based on [] shares of our common stock outstanding as of January 22, 2019.

The number of shares of our common stock to be outstanding after this offering excludes:

• 4,788,347 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2018, at a weighted average exercise price of \$2.82 per share;

• 34,251,014 shares of our common stock issuable upon the exercise of warrants outstanding as of September 30, 2018, at a weighted average exercise price of \$1.07 per share; and

• 2,051,395 shares of our common stock available for future issuance as of September 30, 2018 under our 2015 Equity Incentive Plan.

Unless otherwise indicated, all information in this prospectus supplement assumes:

• no exercise of the outstanding options or warrants described above;

• no vesting of the restricted stock; and

• no exercise by the underwriter of its option to purchase up to additional shares of our common stock.

RISK FACTORS

Before you make a decision to invest in our securities, you should consider carefully the risks described below, together with other information in this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein, including those risks identified under “Item 1A. Risk Factors” in our Annual Report on Form 10-K for the year ended December 31, 2017 and our subsequent Quarterly Reports on Form 10-Q, which are incorporated by reference in this prospectus supplement and which may be amended, supplemented or superseded by other reports that we subsequently file with the SEC. If any of the following events actually occur, our business, operating results, prospects or financial condition could be materially and adversely affected. This could cause the trading price of our common stock to decline and you may lose all or part of your investment. The risks described below are not the only ones that we face. Additional risks not presently known to us or that we currently deem immaterial may also significantly impair our business operations and could result in a complete loss of your investment. Please also read carefully the section entitled “Cautionary Note Regarding Forward-Looking Statements.”

Risks Related to this Offering

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

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds 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 cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

You will experience immediate and substantial dilution in the book value per share of the shares of common stock you purchase in this offering and may experience further dilution in the future.

The public offering price of the common stock offered pursuant to this prospectus supplement is substantially higher than the net tangible book value per share of our common stock. Therefore, you will incur immediate and substantial dilution in the net tangible book value per share of common stock from the public offering price per share of \$. See the section titled “Dilution” on page S-12 below for a more detailed discussion of the dilution investors in this offering will incur if they purchase shares in this offering. In addition, in the past, we issued options and warrants to acquire shares of our common stock. To the extent these options and/or warrants are exercised, you will sustain future dilution.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional shares of common stock or other securities convertible into or exchangeable for our shares of common stock at prices that may not be the same as the prices per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing shareholders. The price per share at which we sell additional shares of common stock, or securities convertible or exchangeable into shares of common stock, in future transactions may be higher or lower than the prices per share paid by investors in this offering.

Sales of substantial amounts of our common stock in the public markets, or the perception that such sales might occur, could reduce the price that our common stock might otherwise attain, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock and may make it more difficult for you to sell your common stock at a time and price that you may deem appropriate. As of September 30, 2018, we had outstanding 58,679,492 shares of common stock. Of these shares, 3,774,129 shares are subject to lock-up agreements entered into in connection with this offering but will be able to be sold beginning on the date that is 90 days after the date of this prospectus supplement. Holders of an aggregate of 27,796,445 shares of our common stock have rights, subject to specified 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. In connection with this offering, the holders of these securities waived these registration rights for a period that ends 90 days after the closing of this offering. We have also filed registration statements registering all shares of common stock that we may issue under our equity compensation plans. These

shares can be freely sold in the public market upon issuance, subject to volume, notice and manner of sale limitations applicable to affiliates and the applicable lock-up agreements entered into in connection with this public offering. See the "Underwriting" section of this prospectus supplement for a description of the lock-up agreements entered into in connection with this offering.

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

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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 your sole source of gain for the foreseeable future.

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 January [], 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 January 22, 2019, our largest stockholder, investment funds affiliated with New Mountain Capital, or the New Mountain Entities, beneficially owned, in the aggregate, approximately 25.7% 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 initial public offering, or 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. See “Certain Relationships and Related Person Transactions-Stockholders Agreements” in our Annual Report on Form 10-K, incorporated herein by reference, for additional information on our stockholder agreement with the New Mountain Entities.

Our second largest stockholder, Puissance, beneficially owned approximately 14.1% of our outstanding common stock as of January 22, 2019.

Our third largest stockholder, Venrock Healthcare, beneficially owned approximately 12.5% of our outstanding common stock as of January 22, 2019.

Our fourth largest stockholder, Linde North America, Inc., an indirect wholly-owned subsidiary of Linde AG, or Linde, beneficially owned approximately 9% of our outstanding common stock, as of January 22, 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 described in “Certain Relationships and Related Person Transactions-Stockholders Agreements” in our Annual Report on Form 10-K, incorporated herein by reference.

The New Mountain Entities 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.

USE OF PROCEEDS

We estimate that the net proceeds from our issuance and sale of shares of our common stock in this offering will be approximately \$ million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriter exercises its option to purchase additional shares in full, we estimate that the net proceeds to us will be approximately \$ million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

As of September 30, 2018, we had cash and cash equivalents of approximately \$19.6 million. We currently estimate that we will use the net proceeds from this offering, together with our existing cash and cash equivalents, to fund working capital and other general corporate purposes and pursuit of our other research and development efforts. This expected use of net proceeds from this offering and our existing cash and cash equivalents represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development, the status of and results from clinical trials, the timing of regulatory submissions and the outcome of regulatory reviews, as well as any collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering. We have no current agreements, commitments or understandings for any material acquisitions or licenses of any third-party products, businesses or technologies.

We expect that the net proceeds from this offering, and our existing cash and cash equivalents described above, will enable us to fund working capital and other general corporate purposes and pursuit of our other research and development efforts. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. See the "Risk Factors" section of this prospectus supplement and the documents incorporated by reference for a discussion of the risks affecting our business that could have an adverse effect on our available capital resources.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

PRICE RANGE OF COMMON STOCK

Our common stock is listed on The Nasdaq Global Market and trades under the symbol "BLPH". The following table sets forth, for the periods indicated, the high and low intraday sales prices of our common stock as reported by The Nasdaq Global Market:

| | High | Low |
|--|---------|---------|
| Year ending December 31, 2019 | | |
| First quarter (through January 22, 2019) | \$ 1.22 | \$ 0.79 |
| Year ended December 31, 2018 | | |
| First quarter | \$ 2.71 | \$ 1.60 |
| Second quarter | \$ 3.30 | \$ 1.84 |
| Third quarter | \$ 2.88 | \$ 0.60 |
| Fourth quarter | \$ 1.26 | \$ 0.63 |
| Year ended December 31, 2017 | | |
| First quarter | \$ 1.98 | \$ 0.52 |
| Second quarter | \$ 1.68 | \$ 1.11 |
| Third quarter | \$ 1.63 | \$ 1.00 |
| Fourth quarter | \$ 2.74 | \$ 1.28 |

On January 22, 2019, the last sale price of our common stock as reported on The Nasdaq Global Market was \$0.88 per share. As of January 22, 2019, we had approximately 233 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees.

DIVIDEND POLICY

We have never declared or paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends in respect of our common stock in the foreseeable future.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and our capitalization as of September 30, 2018: on an actual basis; and

on an as adjusted basis to give effect to our issuance and sale of shares of our common stock in this offering at the public offering price of \$ per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this table together with our financial statements and related notes included in our most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q, each of which is incorporated by reference in this prospectus supplement and the accompanying prospectus.

| | As of September 30, 2018 | |
|--|---|----------------|
| | Actual | As Adjusted |
| | (in thousands, except share and per share data) | |
| Cash and cash equivalents | \$19,552 | \$ [] |
| Marketable securities | 998 | |
| Stockholders' equity: | | |
| Common stock, \$0.01 par value per share; 200,000,000 shares authorized and 58,679,492 shares issued and outstanding at September 30, 2018 | 587 | [] |
| Additional paid-in capital | 178,925 | [] |
| Accumulated other comprehensive loss | (1) | |
| Accumulated deficit | (175,584) | ([]) |
| Total stockholders' equity | 3,927 | [] |
| Total capitalization | \$24,477 | \$ [] |

The table above is based on 58,679,492 shares of common stock outstanding as of September 30, 2018 and does not include:

4,788,347 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2018, at a weighted average exercise price of \$2.82 per share;

34,251,014 shares of our common stock issuable upon the exercise of warrants outstanding as of September 30, 2018, at a weighted average exercise price of \$1.07 per share; and

2,051,395 shares of our common stock available for future issuance as of September 30, 2018 under our 2015 Equity Incentive Plan.

DILUTION

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

Our historical net tangible book value as of September 30, 2018 was \$3.9 million, or \$0.07 per share of our common stock. Our historical net tangible book value is the amount of our total tangible assets less our total liabilities.

Historical net tangible book value per share represents historical net tangible book value divided by the 58,679,492 shares of our common stock outstanding as of September 30, 2018.

After giving effect to our issuance and sale of shares of our common stock in this offering at the public offering price of \$ per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2018 would have been \$ million, or \$ per share.

This represents an immediate increase in as adjusted net tangible book value per share of \$[] to existing stockholders and immediate dilution of \$ in as adjusted net tangible book value per share to new investors purchasing common stock in this offering. Dilution per share to new investors is determined by subtracting as adjusted net tangible book value per share after this offering from the public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis:

| | |
|--------------------------|----|
| Offering price per share | \$ |
|--------------------------|----|

| | |
|---|--|
| Historical net tangible book value per share as of September 30, 2018 | |
|---|--|

| | |
|--|--|
| Increase in as adjusted net tangible book value per share attributable to new investors purchasing shares in this offering | |
|--|--|

| | |
|---|--|
| As adjusted net tangible book value per share after this offering | |
|---|--|

| | |
|--|--|
| Dilution per share to new investors purchasing shares in this offering | |
|--|--|

The table above is based on 58,679,492 shares of common stock outstanding as of September 30, 2018 and does not include:

4,788,347 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2018, at a weighted average exercise price of \$2.82 per share;

34,251,014 shares of our common stock issuable upon the exercise of warrants outstanding as of September 30, 2018, at a weighted average exercise price of \$1.07 per share; and

2,922,750 shares of our common stock available for future issuance as of September 30, 2018 under our 2015 Equity Incentive Plan.

If any additional shares are issued in connection with the exercise of options or warrants, or if the underwriter exercises its option to purchase additional shares of our common stock, you will experience further dilution.

MATERIAL U.S. TAX CONSIDERATIONS FOR NON-U.S. HOLDERS OF COMMON STOCK

The following is a discussion of the material U.S. federal income and estate tax considerations relating to the ownership and disposition of shares of our common stock purchased in this offering by a non-U.S. holder. For purposes of this discussion, the term "non-U.S. holder" means a beneficial owner (other than a partnership or other pass-through entity) of our common stock that is not, for U.S. federal income tax purposes:

• an individual who is a citizen or resident of the United States;

• a corporation, or other entity treated as a corporation, created or organized in or under the laws of the United States or of any political subdivision of the United States;

• an estate, the income of which is subject to U.S. federal income taxation regardless of its source; or

a trust, if a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or if the trust has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a U.S. person.

This discussion does not address the tax treatment of partnerships or other entities that are pass-through entities for U.S. federal income tax purposes or persons who hold our common stock through partnerships or such other pass-through entities. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its own tax advisor regarding the tax consequences of acquiring, holding and disposing of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus supplement and all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change or differing interpretation could alter the tax consequences to non-U.S. holders described in this prospectus supplement. In addition, the Internal Revenue Service, or the IRS, could challenge one or more of the tax consequences described in this prospectus supplement.

We assume in this discussion that each non-U.S. holder holds shares of our common stock as a capital asset (generally, property held for investment) for U.S. federal income tax purposes. This discussion does not address all aspects of U.S. federal income and estate taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances, nor does it address any aspects of U.S. state, local or non-U.S. taxes, the alternative minimum tax, or the Medicare tax on net investment income. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

• insurance companies;

• tax-exempt organizations;

• financial institutions;

• brokers or dealers in securities;

• pension plans;

• controlled foreign corporations;

• passive foreign investment companies;

• non-U.S. governments;

owners that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment or who have elected to mark securities to market; and

certain U.S. expatriates.

THIS DISCUSSION IS FOR INFORMATION ONLY AND IS NOT, AND IS NOT INTENDED TO BE, LEGAL OR TAX ADVICE. PROSPECTIVE INVESTORS SHOULD CONSULT THEIR OWN TAX ADVISORS REGARDING

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THE U.S. FEDERAL, STATE, LOCAL, ESTATE AND NON-U.S. INCOME AND OTHER TAX CONSIDERATIONS OF ACQUIRING, HOLDING AND DISPOSING OF OUR COMMON STOCK.

Distributions

As discussed under "Dividend Policy" above, we do not currently expect to make distributions in respect of our common stock. If we make distributions in respect of our common stock, those distributions generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles, subject to the tax treatment described in this section. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of capital, up to the holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below under the heading "Gain on Sale, Exchange or Other Taxable Disposition of Our Common Stock." Any such distributions will also be subject to the discussions below under the headings "Information Reporting and Backup Withholding" and "FATCA."

Dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States, and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements (generally including provision of a valid IRS Form W-8ECI (or applicable successor form) certifying that the dividends are effectively connected with the non-U.S. holder's conduct of a trade or business within the United States). However, such U.S. effectively connected income, net of specified deductions and credits, is taxed in the hands of the non-U.S. holder at the same graduated U.S. federal income tax rates as would apply if such holder were a U.S. person (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is classified as a corporation for U.S. federal income tax purposes may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) and satisfy applicable certification and other requirements.

Non-U.S. holders are urged to consult their own tax advisors regarding their entitlement to benefits under a relevant income tax treaty and the specific methods available to them to satisfy these requirements.

A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim for a refund with the IRS.

Gain on Sale, Exchange or Other Taxable Disposition of Our Common Stock

Subject to the discussions below under the headings "Information Reporting and Backup Withholding" and "FATCA," a non-U.S. holder generally will not be subject to U.S. federal income tax or withholding tax on any gain realized upon such non-U.S. holder's sale, exchange or other taxable disposition of our common stock unless:

the gain is effectively connected with the non-U.S. holder's conduct of a trade or business in the United States, and, if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States; in these cases, the non-U.S. holder will be taxed on a net income basis at the graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code) with respect to the gain, and, if the non-U.S. holder is a foreign corporation, an additional branch profits tax at a rate of 30% (or a lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence) may also apply;

the non-U.S. holder is a non-resident alien present in the United States for 183 days or more in the taxable year of the disposition and certain other requirements are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's

country of residence) on the net gain derived from the disposition, which may be offset by certain U.S.-source capital losses of the non-U.S. holder, if any; or

we are or have been, at any time during the five-year period preceding such disposition (or the non-U.S. holder's holding period, if shorter) a "U.S. real property holding corporation," unless our common stock is regularly traded on an established securities market and the non-U.S. holder held no more than 5% of our outstanding common stock, directly or indirectly, during the shorter of the five-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. If we are determined to be a U.S. real property holding corporation and

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the foregoing exception does not apply, then the non-U.S. holder generally will be taxed on its net gain derived from the disposition at the graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code). Generally, a corporation is a "U.S. real property holding corporation" only if the fair market value of its "U.S. real property interests" (as defined in the Code and applicable regulations) equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a "U.S. real property holding corporation" for U.S. federal income tax purposes or that we are likely to become one in the future. No assurance can be provided that our common stock will continue to be regularly traded on an established securities market for purposes of the rules described above.

Information Reporting and Backup Withholding

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders generally will have to comply with specific certification procedures to establish that the holder is not a U.S. person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Generally, a holder will comply with such procedures if it provides a properly executed IRS Form W-8BEN or W-8BEN-E (or other applicable Form W-8), or otherwise meets documentary evidence requirements for establishing that it is a non-U.S. holder, or otherwise establishes an exemption. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above under "Distributions," will generally be exempt from U.S. backup withholding.

Information reporting and backup withholding generally will apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or non-U.S., unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is timely filed with the IRS.

U.S. Federal Estate Tax

Shares of our common stock owned or treated as owned by an individual who is not a citizen or resident of the United States (as specially defined for U.S. federal estate tax purposes) at the time of death are considered U.S. situs assets and will be included in the individual's gross estate for U.S. federal estate tax purposes. Such shares, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise.

FATCA

Provisions of the Code commonly referred to as the Foreign Account Tax Compliance Act, or FATCA, generally impose a 30% withholding tax on dividends on, and gross proceeds from the sale or disposition of, our common stock if paid to a foreign entity unless (i) if the foreign entity is a "foreign financial institution," the foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a "foreign financial institution," the foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt under FATCA.

Withholding under FATCA generally (1) applies to payments of dividends on our common stock, and (2) will apply to payments of gross proceeds from a sale or other disposition of our common stock made after December 31, 2018. An intergovernmental agreement between the United States and an applicable foreign country may modify the

requirements described in this section. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of the tax. Non-U.S. holders should consult their own tax advisors regarding the possible implications of FATCA on their investment in our common stock and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30% withholding tax under FATCA.

The preceding discussion of material U.S. federal tax considerations is for information only. It is not legal or tax advice. Prospective investors should consult their own tax advisors regarding the particular U.S. federal, state, local and non-

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U.S. tax consequences of acquiring, holding and disposing of our common stock, including the consequences of any proposed changes in applicable laws.

UNDERWRITING

We have entered into an underwriting agreement dated , 2019 with H.C. Wainwright & Co., LLC, as underwriter, with respect to the shares of common stock being offered hereby.

Pursuant to the terms and subject to the conditions contained in the underwriting agreement, we have agreed to sell to the underwriter, and the underwriter has agreed to purchase from us, the number of shares of common stock set forth opposite its name below:

| Underwriter | Number of Shares of Common Stock |
|----------------------------|--|
| H.C. Wainwright & Co., LLC | |

The underwriting agreement provides that the obligation of the underwriter to purchase the shares of common stock offered by this prospectus supplement and the accompanying prospectus is subject to certain conditions. The underwriter is obligated to purchase all of the shares of common stock offered hereby if any of these shares are purchased.

Over-Allotment Option

We have granted to the underwriter an option to purchase up to an additional shares of common stock from us at the same price to the public, and with the same underwriting discount, as set forth above. The underwriter may exercise this option any time during the 45-day period after the date of this prospectus.

Discounts, Commissions and Expenses

The underwriter proposes to offer the shares of common stock purchased pursuant to the underwriting agreement to the public at the public offering price set forth on the cover page of this prospectus supplement and to certain dealers at that price less a concession not in excess of \$ per share, based on the public offering price per share set forth on the cover page of this prospectus supplement. After this offering, the public offering price and concession may be changed by the underwriter. No such change shall change the amount of proceeds to be received by us as set forth on the cover page of this prospectus supplement.

In connection with the sale of the common stock to be purchased by the underwriter, the underwriter will be deemed to have received compensation in the form of underwriting commissions and discounts. The underwriter's commissions and discounts will be 7% of the gross proceeds of this offering, or \$ per share.

The underwriter has advised us that it does not intend to confirm sales to any accounts over which it exercises discretionary authority.

The following table shows the underwriting discounts and commissions payable to the underwriter by us in connection with this offering:

| | Total (no exercise) | Total (full exercise) |
|--|------------------------|-----------------------|
| Public offering price | | |
| Underwriting discounts and commissions payable by us | | |
| Proceeds, before expenses, to us | | |

We have also agreed to reimburse the underwriter for reasonable out-of-pocket expenses, including legal fees and expenses, of up to \$100,000, to provide the underwriter with a \$25,000 non-accountable expense allowance and \$10,000 for the clearing expenses of the underwriter in connection with this offering. We estimate the total expenses payable by us for this offering will be approximately \$, which amount excludes the underwriting discount and commissions.

Listing

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

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No Sales of Similar Securities

We and each of our executive officers and our directors have agreed to certain restrictions on our ability to sell additional shares of our common stock for a period of 90 days after the date of this prospectus supplement. We have agreed not to directly or indirectly offer for sale, sell, contract to sell, grant any option for the sale of, or otherwise issue or dispose of, any shares of common stock, options or warrants to acquire shares of common stock, or any related security or instrument, without the prior written consent of H.C. Wainwright & Co., LLC. The agreements provide exceptions for (1) sales to underwriters pursuant to the underwriting agreement, (2) our sales in connection with the exercise of options granted and the granting of options to purchase shares of our common stock under the our existing stock option plans and (3) certain other exceptions.

Stabilization

To facilitate the offering, the underwriter may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock during and after the offering. Specifically, the underwriter may over-allot or otherwise create a short position in the common stock for their own account by selling more shares of common stock than have been sold to them by us. The underwriter may elect to cover any such short position by purchasing shares of common stock in the open market or by exercising the option granted to the underwriter. In addition, the underwriter may stabilize or maintain the price of the common stock by bidding for or purchasing shares of common stock in the open market and may impose penalty bids. If penalty bids are imposed, selling concessions allowed to syndicate members or other broker-dealers participating in the offering are reclaimed if shares of common stock previously distributed in the offering are repurchased, whether in connection with stabilization transactions or otherwise. The effect of these transactions may be to stabilize or maintain the market price of the common stock at a level above that which might otherwise prevail in the open market. The imposition of a penalty bid may also effect the price of the common stock to the extent that it discourages resales of the common stock. The magnitude or effect of any stabilization or other transactions is uncertain. These transactions may be effected on the Nasdaq National Market or otherwise and, if commenced, may be discontinued at any time.

In connection with this offering, the underwriter may also engage in passive market making transactions in the common stock on the Nasdaq National Market. Passive market making consists of displaying bids on the Nasdaq National Market limited by the prices of independent market makers and effecting purchases limited by those prices in response to order flow. Rule 103 of Regulation M promulgated by the SEC limits the amount of net purchases that each passive market maker may make and the displayed size of each bid. Passive market making may stabilize the market price of the common stock at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

Other Activities and Relationships

H.C. Wainwright & Co., LLC and certain of its affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. H.C. Wainwright & Co., LLC and certain of its affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which it received or will receive customary fees and expenses.

NOTICE TO INVESTORS

Canada

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

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

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the issuer and the underwriter are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Australia

This prospectus is not a disclosure document for the purposes of Australia's Corporations Act 2001 (Cth) of Australia, or Corporations Act, has not been lodged with the Australian Securities & Investments Commission and is only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus in Australia:

You confirm and warrant that you are either:

• "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;

• a "sophisticated investor" under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to the company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made; or

• a "professional investor" within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor or professional investor under the Corporations Act any offer made to you under this prospectus is void and incapable of acceptance. You warrant and agree that you will not offer any of the shares issued to you pursuant to this prospectus for resale in Australia within 12 months of those securities being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

European Economic Area

In relation to each member state of the European Economic Area which has implemented the Prospectus Directive, each referred to herein as a Relevant Member State, with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State, referred to herein as the Relevant Implementation Date, no offer of any securities which are the subject of the offering contemplated by this prospectus has been or will be made to the public in that Relevant Member State other than any offer where a prospectus has been or will be published in relation to such securities that has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the relevant competent authority in that Relevant Member State in accordance with the Prospectus Directive, except that with effect from and including the Relevant Implementation Date, an offer of such securities may be made to the public in that Relevant Member State:

• to any legal entity which is a "qualified investor" as defined in the Prospectus Directive;

to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the underwriter for any such offer; or

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in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of securities shall require the Company or the underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive. For the purposes of this provision, the expression an "offer to the public" in relation to any securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe the securities, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

Hong Kong

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32) of Hong Kong. No document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance.

This prospectus has not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

Japan

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended), or FIEL, and the Initial Purchaser will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means, unless otherwise provided herein, any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

This prospectus has not been and will not be lodged or registered with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or the invitation for subscription or purchase of the securities may not be issued, circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to the public or any member of the public in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person as defined under Section 275(2), or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions, specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of any other applicable provision of the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:
a corporation (which is not an accredited investor as defined under Section 4A of the SFA) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor,

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shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for six months after that corporation or that trust has acquired the Offer Shares under Section 275 of the SFA except:

to an institutional investor under Section 274 of the SFA or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than \$200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions, specified in Section 275 of the SFA;

•where no consideration is given for the transfer; or

•where the transfer is by operation of law.

Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus nor any other offering or marketing material relating to the offering, the Company or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, or FINMA, and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

Israel

This document does not constitute a prospectus under the Israeli Securities Law, 5728-1968, or the Securities Law, and has not been filed with or approved by the Israel Securities Authority. In the State of Israel, this document is being distributed only to, and is directed only at, and any offer of the shares is directed only at, investors listed in the first addendum, or the Addendum, to the Israeli Securities Law, consisting primarily of joint investment in trust funds, provident funds, insurance companies, banks, portfolio managers, investment advisors, members of the Tel Aviv Stock Exchange, underwriters, venture capital funds, entities with equity in excess of NIS 50 million and "qualified individuals", each as defined in the Addendum (as it may be amended from time to time), collectively referred to as qualified investors (in each case purchasing for their own account or, where permitted under the Addendum, for the accounts of their clients who are investors listed in the Addendum). Qualified investors will be required to submit written confirmation that they fall within the scope of the Addendum, are aware of the meaning of same and agree to it.

United Kingdom

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

This prospectus and its contents should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a Relevant

Person should not act or rely on this document or any of its contents.

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LEGAL MATTERS

The validity of the shares of common stock offered hereby is being passed upon for us by Mintz, Levin, Cohn, Ferris, Glovsky & Popeo, P.C., New York, New York. Ellenoff Grossman & Schole LLP, New York, New York is acting as counsel for H.C. Wainwright & Co., LLC in connection with this offering.

EXPERTS

The consolidated financial statements of Bellerophon Therapeutics, Inc. (formerly Bellerophon Therapeutics LLC) as of December 31, 2017 and 2016, and for each of the years in the three-year period ended December 31, 2017, have been incorporated by reference herein in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at <http://www.sec.gov>. Copies of certain information filed by us with the SEC are also available on our website at <http://www.bellerophon.com>. Our website is not a part of this prospectus supplement and accompanying prospectus and is not incorporated by reference in this prospectus supplement. You may also read and copy any document we file at the SEC's Public Reference Room, 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

This prospectus supplement is part of a registration statement we filed with the SEC. This prospectus supplement and the accompanying prospectus omit some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information on us and the securities we are offering. Statements in this prospectus supplement and the accompanying prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC's Internet site.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus supplement and the accompanying prospectus is considered to be part of this prospectus supplement and the accompanying prospectus. Because we are incorporating by reference future filings with the SEC, those future filings may modify or supersede some of the information included or incorporated in this prospectus supplement and the accompanying prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus supplement, the accompanying prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus supplement and the accompanying prospectus incorporate by reference the documents listed below (File No. 001-36845) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended (in each case, other than those documents or the portions of those documents not deemed to be filed), until the offering of the securities under the registration statement is terminated or completed:

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our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, filed with the SEC on March 15, 2018, as amended on May 17, 2018, including the information specifically incorporated by reference into the Annual Report on Form 10-K from our definitive proxy statement for the 2018 Annual Meeting of Stockholders;

our Quarterly Report on Form 10-Q for the period ended September 30, 2018, filed with the SEC on November 7, 2018

our Quarterly Report on Form 10-Q for the period ended June 30, 2018, filed with the SEC on August 1, 2018;

our Quarterly Report on Form 10-Q for the period ended March 31, 2018, filed with the SEC on May 10, 2018;

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- Current Reports on Form 8-K filed on January 17, 2018, March 26, 2018, April 26, 2018, May 24, 2018, August 7, 2018, August 13, 2018, September 27, 2018, October 24, 2018, and January 7, 2019, and

The description of our common stock contained in our Registration Statement on Form 8-A filed on February 10, 2015, including any amendments or reports filed for the purpose of updating such description.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number:

Bellerophon Therapeutics, Inc.
Attn: Chief Financial Officer
184 Liberty Corner Road, Suite 302
Warren, New Jersey 07059
(908) 574-4770

Filed Pursuant to Rule 424(b)(2)
Registration File No. 333-225878

PROSPECTUS

BELLEROPHON THERAPEUTICS, INC.

\$100,000,000

COMMON STOCK
PREFERRED STOCK
DEBT SECURITIES
WARRANTS
RIGHTS
UNITS

This prospectus will allow us to issue, from time to time at prices and on terms to be determined at or prior to the time of the offering, up to \$100,000,000 of any combination of the securities described in this prospectus, either individually or in units. We may also offer common stock or preferred stock upon conversion of or exchange for the debt securities; common stock or preferred stock or debt securities upon the exercise of warrants or rights.

This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide you with the specific terms of any offering in one or more supplements to this prospectus. The prospectus supplements will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this document. You should read this prospectus and any prospectus supplement, as well as any documents incorporated by reference into this prospectus or any prospectus supplement, carefully before you invest.

Our securities may be sold directly by us to you, through agents designated from time to time or to or through underwriters or dealers. For additional information on the methods of sale, you should refer to the section entitled “Plan of Distribution” in this prospectus and in the applicable prospectus supplement. If any underwriters or agents are involved in the sale of our securities with respect to which this prospectus is being delivered, the names of such underwriters or agents and any applicable fees, commissions or discounts and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds that we expect to receive from such sale will also be set forth in a prospectus supplement.

Our common stock is listed on the Nasdaq Global Market, under the symbol “BLPH.” On June 22, 2018, the last reported sale price of our common stock on the Nasdaq Global Market was \$2.87 per share.

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks that we have described on page 7 of this prospectus under the caption “Risk Factors.” We may include specific risk factors in supplements to this prospectus under the caption “Risk Factors.” This prospectus may not be used to sell our securities unless accompanied by a prospectus supplement.

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

The date of this prospectus is July 6, 2018.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, utilizing a “shelf” registration process. Under this shelf registration process, we may offer shares of our common stock, preferred stock, various series of debt securities and/or warrants or rights to purchase any of such securities, either individually or in units, in one or more offerings, with a total value of up to \$100,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will contain specific information about the terms of that offering.

This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of the offering of the securities, you should refer to the registration statement, including its exhibits. The prospectus supplement may also add, update or change information contained or incorporated by reference in this prospectus. However, no prospectus supplement will offer a security that is not registered and described in this prospectus at the time of its effectiveness. This prospectus, together with the applicable prospectus supplements and the documents incorporated by reference into this prospectus, includes all material information relating to the offering of securities under this prospectus. You should carefully read this prospectus, the applicable prospectus supplement, the information and documents incorporated herein by reference and the additional information under the heading “Where You Can Find More Information” before making an investment decision.

You should rely only on the information we have provided or incorporated by reference in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained or incorporated by reference in this prospectus. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus or any prospectus supplement is accurate only as of the date on the front of the document and that any information we have incorporated herein by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or any sale of a security.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

This prospectus may not be used to consummate sales of our securities, unless it is accompanied by a prospectus supplement. To the extent there are inconsistencies between any prospectus supplement, this prospectus and any documents incorporated by reference, the document with the most recent date will control.

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.

Unless the context otherwise requires, “Bellerophon,” “the Company,” “we,” “us,” “our” and similar terms refer to Bellerophon Therapeutics, Inc.

PROSPECTUS SUMMARY

The following is a summary of what we believe to be the most important aspects of our business and the offering of our securities under this prospectus. We urge you to read this entire prospectus, including the more detailed consolidated financial statements, notes to the consolidated financial statements and other information incorporated by reference from our other filings with the SEC or included in any applicable prospectus supplement. Investing in our securities involves risks. Therefore, carefully consider the risk factors set forth in any prospectus supplements and in our most recent annual and quarterly filings with the SEC, as well as other information in this prospectus and any prospectus supplements and the documents incorporated by reference herein or therein, before purchasing our securities. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities.

Overview

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

Our Development Program

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

From the inception of our business through December 31, 2017, \$261.7 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 chronic thromboembolic PH, or CTEPH, PH associated with sarcoidosis and PH associated with pulmonary edema from high altitude sickness with a royalty equal to 5% of net sales of any commercial products for these three additional indications. In November 2015, we entered into an amendment to our exclusive cross-license, technology transfer and regulatory matters agreement with Ikaria that included a royalty equal to 3% of net sales of any

commercial products for PAH. Our INOpulse program is built on scientific and technical expertise developed for the therapeutic delivery of inhaled nitric oxide. In 2010 and 2012, respectively, Ikaria submitted investigational new drug applications, or INDs, for INOpulse for the treatment of patients with PAH and PH-COPD. PAH is a form of PH that is closely related to persistent PH of the newborn. These INDs were included in the assets that were transferred to us by Ikaria.

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

Inhaled nitric oxide is widely used in the hospital setting for the treatment of a variety of conditions and, as reported by Ikaria, over 600,000 patients have been treated with inhaled nitric oxide worldwide since its first such use. However, chronic outpatient use of this therapy has previously been limited by a lack of a safe and compact delivery system for outpatient use. We have designed our INOpulse device, which is the means by which inhaled nitric oxide is delivered to the patient, to be portable, which enables use by ambulatory patients on a daily basis inside or outside their homes. Our INOpulse device has a proprietary mechanism that delivers brief, targeted pulses of nitric oxide timed to occur at the beginning of a breath for delivery to the well-ventilated alveoli of the lungs, which minimizes the amount of drug required for treatment. We estimate this, and the higher concentration of nitric oxide we use, reduces the volume of drug delivered to approximately 5% of the volume required for equivalent alveolar absorption using standard continuous flow delivery systems, and also reduces the amount of nitric oxide, as well as its by-product nitrogen dioxide, that is exhaled and released into the patient's environment. INOpulse is designed to automatically adjust nitric oxide delivery based on a patient's breathing pattern to deliver a constant and 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 have begun using our second generation device, which we refer to as the INOpulse device. The INOpulse device has approximately the same dimensions as a paperback book and weighs approximately 2.5 pounds. The INOpulse device has a simple and intuitive user interface and a battery life of approximately 16 hours when recharged, which takes approximately four hours and can be done while the patient sleeps. Based on the doses we have evaluated in our clinical trials, we expect that most patients will use two cartridges a day. The INOpulse device incorporates our proprietary triple-lumen nasal cannula, safety systems and proprietary software algorithms. The triple-lumen nasal cannula enables more accurate dosing of nitric oxide and minimizes infiltration of oxygen, which can react with nitric oxide to form nitrogen dioxide. Our triple-lumen nasal cannula consists of a thin, plastic tube that is divided into three channels from end-to-end, including at the prongs that are placed in the patient's nostrils, with one channel delivering inhaled nitric oxide, a second for breath detection and a third available for oxygen delivery. INOpulse is configured to be highly portable and compatible with long-term oxygen therapy, or LTOT, systems via nasal cannula delivery.

The INOpulse device has been well received by patients in the usability research we have conducted. In addition to the baseline testing on the original INOpulse DS device, we have conducted two rounds of testing with COPD and PAH patients to evaluate the user interface, loading mechanism, size, carrying bag and other features. In the usability research we have conducted, all eight patients with experience with the INOpulse DS device responded positively to the INOpulse device, and several of these patients indicated that the ability to take the INOpulse device outside the home would likely reduce concerns with maintaining compliance. 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-IPF, CTEPH, PH associated with sarcoidosis and PH associated with pulmonary edema from altitude sickness which, collectively, we refer to as the Bellerophon indications. These include patents with respect to the pulsed delivery of nitric oxide to ensure a consistent dose over time, which expire as late as 2027 in the United States and as

late as 2026 in certain other countries, as well as with respect to the special triple-lumen cannula that allows for safer and more accurate dosing of pulsed nitric oxide, which expires in 2033 in the United States and abroad. We have also licensed several other patent applications from Ikaria for certain of the innovations included in the INOpulse device and certain of the resulting patents, if issued, would expire as late as 2030 in the United States. 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. This certification covers the design, development and manufacture of inhaled pulsatile nitric oxide drug delivery systems including our triple-lumen cannula and application software.

INOpulse for PAH

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

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

We completed a randomized, placebo-controlled, double-blind Phase 2 clinical trial of INOpulse for PAH in October 2014, which was Part 1 of the trial. In February 2016, we announced positive data from the final analysis of Part 2 of our Phase 2 clinical trial of INOpulse for PAH. The data 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 are moving forward with Phase 3 development. 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 has been 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 study, and a second confirmatory randomized withdrawal study with approximately 40 patients who will be crossing over from the INOvation-1 study, can serve as the two adequate and well-controlled studies to support a NDA filing for INOpulse in PAH subjects on LTOT. Both studies include an interim analysis approximately half-way through each study to assess for efficacy and futility. The interim analysis for the INOvation-1 study also includes a potential sample size reassessment. In January 2018, we announced our INOvation-1 study enrollment exceeded 100 patients, representing more than half of the anticipated enrollment.

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. The FDA asked us to confirm the dose range and the safety related to hypoxemia in PH-COPD patients using the INOpulse device, prior to proceeding to large scale trials. Following this guidance, we conducted a Phase 2 acute dose ranging randomized placebo-controlled trial in 159 patients with the INOpulse DS device, with doses ranging from 3 mcg to 75 mcg. This trial, which we completed in July

2014, identified a dose range that showed similar reduction in pulmonary arterial pressure versus baseline when compared to the initial acute effects of pulsed inhaled nitric oxide in the original chronic-use trial. In addition, in our confirmatory trial, none of the INOpulse doses tested had an adverse effect on hypoxemia relative to placebo. While the reduction in pulmonary arterial pressure did not reach statistical significance versus placebo in this acute setting, which was the primary endpoint of the trial, we believe that the results have confirmed a dose range for this therapy that delivers a significant reduction in pulmonary arterial pressure versus baseline and does not cause hypoxemia in patients with PH-COPD. In September 2015, an oral presentation of late-breaking data from a clinical trial sponsored by us was presented at the European Respiratory Society International Congress 2015 in Amsterdam. The data showed that INOpulse improved vasodilation in patients with PH-COPD. 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 during 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, and enrolled the first patient in October 2016. In May 2018, we announced that we reached agreement with the FDA on all key aspects of our planned Phase 2b study of INOpulse for treatment of PH-COPD.

INOpulse for PH-ILD

We are also developing INOpulse for the treatment of PH-ILD. 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 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 blood circulation, 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 IPF, a progressive disease of unknown etiology associated with growth of fibrotic tissue in the lungs causing hypoxemia, dyspnea, fatigue and cough. The median survival is only two to three years. Based on academic studies, we estimate the prevalence of IPF in the United States at approximately 90,000 patients, with 20-40% suffering from pulmonary hypertension. PH with IPF increases mortality. The presence of PH correlates most closely with the need for oxygen therapy. The two therapies that are currently approved for IPF, Nintedanib and Pirfenidone, cost approximately \$100,000 per year.

iNO may improve outcomes in 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. However, the arterial oxygen tension (PaO₂) did not improve. The combined inhalation of nitric oxide and oxygen produced a significant decrease of pulmonary arterial pressure (p<0.01) as well as an improvement (p<0.05) in PaO₂ as compared to oxygen alone. These findings support the potential for the combined use of nitric oxide and oxygen for treating idiopathic pulmonary fibrosis patients with pulmonary hypertension.

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. It also assessed the chronic effects of iNO on exercise capacity showing an average 75 meter improvement in 6MWD, and consistent improvement of approximately 80 m% in composite

endpoints of 6MWD and oxygen saturation with four weeks of treatment. 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 PF. PH. In January 2018, we announced the first patient enrollment in our iNO-PF Phase 2b trial.

BCM

In December 2011, we initiated a clinical trial of BCM, which we refer to as our PRESERVATION I trial, and completed enrollment in December 2014. Top-line results from the randomized, double-blind, placebo-controlled clinical trial were announced in July 2015. Topline results showed no statistically significant treatment differences between patients treated with BCM and patients treated with placebo for both the primary and the secondary endpoints. Following the results, we are considering further exploratory work but we do not intend to proceed with further clinical development of BCM at this point until and unless we can determine an alternative path forward. We continue to maintain the patent portfolio, including the composition of matter and method manufacturing patents that we have in-licensed from BioLineRx Ltd.

Our Strategy

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

Advance the clinical development of INOpulse. One of our lead indications for our product candidate is INOpulse for PAH. Our Phase 3 PAH program for INOpulse will include two confirmatory clinical trials including the ongoing INOvation-1 trial and a second confirmatory randomized withdrawal study. We also completed Phase 2 studies for INOpulse in PH-COPD looking at the effect of chronic use on exercise capacity and in PH-IPF consisting of an exploratory acute hemodynamic study.

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

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

The Spin-Out

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.

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

innovative approach to the pulsed delivery of nitric oxide, originated at Ikaria, and we in-licensed BCM while we were a part of 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. In April 2018, we amended the cross-license to (i) remove previous references to IPF and replacing them with references to PF and (ii) include a provision pursuant to which the Company agrees to pay to Ikaria one percent (1%) of PF net sales.

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.

Corporate Information

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

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

Offerings Under This Prospectus

Under this prospectus, we may offer shares of our common stock, preferred stock, various series of debt securities and/or warrants or rights to purchase any of such securities, either individually or in units, with a total value of up to \$100,000,000, from time to time at prices and on terms to be determined by market conditions at the time of the offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

The prospectus supplement also may add, update or change information contained in this prospectus or in documents we have incorporated by reference into this prospectus. However, no prospectus supplement will fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

We may sell the securities directly to investors or to or through agents, underwriters or dealers. We, and our agents or underwriters, reserve the right to accept or reject all or part of any proposed purchase of securities. If we offer securities through agents or underwriters, we will include in the applicable prospectus supplement:

- the names of those agents or underwriters;
- applicable fees, discounts and commissions to be paid to them;
- details regarding over-allotment options, if any; and

the net proceeds to us.

This prospectus may not be used to consummate a sale of any securities unless it is accompanied by a prospectus supplement.

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RISK FACTORS

Please carefully consider the risk factors described in our periodic reports filed with the SEC, which are incorporated by reference in this prospectus. Before making an investment decision, you should carefully consider these risks as well as other information we include or incorporate by reference in this prospectus or include in any applicable prospectus supplement. Additional risks and uncertainties not presently known to us or that we deem currently immaterial may also impair our business operations or adversely affect our results of operations or financial condition.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this prospectus, 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 prospectus 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;

- our ability to continue as a going concern within one year beyond the filing of our Quarterly Report on Form 10-Q for the quarter ended March 31, 2018;

- 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 prospectus, particularly in the “Risk Factors” section, as well as the risk factors incorporated by reference in this prospectus, discussed under “Item 1A-Risk Factors”

in our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, and under similar headings in our subsequently filed quarterly reports on Form 10-Q and annual reports on Form 10-K, 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 prospectus and the documents that we have filed as exhibits to this prospectus 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 prospectus 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.

RATIO OF EARNINGS TO FIXED CHARGES

Any time debt securities are offered pursuant to this prospectus, we will provide a table setting forth our ratio of earnings to fixed charges on a historical basis in the applicable prospectus supplement, if required.

USE OF PROCEEDS

We cannot assure you that we will receive any proceeds in connection with securities which may be offered pursuant to this prospectus. Unless otherwise indicated in the applicable prospectus supplement, we intend to use any net proceeds from the sale of securities under this prospectus for our operations and for other general corporate purposes, including, but not limited to, our internal research and development programs and the development of new programs, general working capital and possible future acquisitions. We have not determined the amounts we plan to spend on any of the areas listed above or the timing of these expenditures. As a result, our management will have broad discretion to allocate the net proceeds, if any, we receive in connection with securities offered pursuant to this prospectus for any purpose. Pending application of the net proceeds as described above, we may initially invest the net proceeds in short-term, investment-grade, interest-bearing securities or apply them to the reduction of short-term indebtedness.

PLAN OF DISTRIBUTION

General Plan of Distribution

We may offer securities under this prospectus from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities (1) through underwriters or dealers, (2) through agents or (3) directly to one or more purchasers, or through a combination of such methods. We may distribute the securities from time to time in one or more transactions at:

• fixed price or prices, which may be changed from time to time;

• market prices prevailing at the time of sale;

• prices related to the prevailing market prices; or

• negotiated prices.

We may directly solicit offers to purchase the securities being offered by this prospectus. We may also designate agents to solicit offers to purchase the securities from time to time. We will name in a prospectus supplement any underwriter or agent involved in the offer or sale of the securities.

If we utilize a dealer in the sale of the securities being offered by this prospectus, we will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

If we utilize an underwriter in the sale of the securities being offered by this prospectus, we will execute an underwriting agreement with the underwriter at the time of sale, and we will provide the name of any underwriter in the prospectus supplement which the underwriter will use to make re-sales of the securities to the public. In connection with the sale of the securities, we, or the purchasers of the securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and the underwriter may compensate those dealers in the form of discounts, concessions or commissions.

With respect to underwritten public offerings, negotiated transactions and block trades, we will provide in the applicable prospectus supplement information regarding any compensation we pay to underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act of 1933, as amended, or the Securities Act, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when

authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

• the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and

if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Shares of our common stock sold pursuant to the registration statement of which this prospectus is a part will be authorized for quotation and trading on the Nasdaq Global Market. The applicable prospectus supplement will contain information, where applicable, as to any other listing, if any, on the Nasdaq Global Market or any securities market or other securities exchange of the securities covered by the prospectus supplement. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

In order to facilitate the offering of the securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than we sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing the applicable security in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if the securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

In compliance with the guidelines of the Financial Industry Regulatory Authority, Inc., or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

The underwriters, dealers and agents may engage in other transactions with us, or perform other services for us, in the ordinary course of their business.

DESCRIPTION OF CAPITAL STOCK

General

The following description of our capital stock and provisions of our restated certificate of incorporation and amended and restated bylaws are summaries and are qualified by reference to the restated certificate of incorporation and the amended and restated bylaws that are on file with the SEC.

Our authorized capital stock consists of 200,000,000 shares of our common stock, \$0.01 par value per share, and 5,000,000 shares of our preferred stock, \$0.01 par value per share, all of which preferred stock is undesignated.

As of June 18, 2018, we had issued and outstanding:

57,610,541 shares of our voting and non-voting common stock held by 226 stockholders of record; and

options to purchase 4,797,347 shares of our non-voting common stock, at a weighted average exercise price of \$2.83 per share.

Common Stock

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

In the event of our liquidation or dissolution, the holders of our common stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any of our outstanding preferred stock. Holders of our common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our preferred stock that we may designate and issue in the future.

Preferred Stock

Under the terms of our restated certificate of incorporation, our board of directors is authorized to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of our outstanding voting stock. There are no shares of preferred stock currently outstanding, and we have no present plans to issue any shares of preferred stock.

Options

As of June 18, 2018, we had outstanding options to purchase 4,797,347 shares of our non-voting common stock, at a weighted average exercise price of \$2.83 per share.

Stockholders Agreements

New Mountain Stockholders Agreement

In February 2015, in connection with our IPO, we entered into a stockholders agreement with the investment funds affiliated with New Mountain Capital, or the New Mountain Entities, which provides that the New Mountain Entities are entitled to designate one director for nomination to our board of directors, to designate one director to the board of directors (or equivalent governing body) of each of our subsidiaries and to appoint the lead director of our board of directors, in each case,

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

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

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

- consolidate or merge into or with any other person, sell, lease or transfer all or a significant portion of our assets or capital stock to another person or enter into any other similar business combination transaction, or effect a liquidation;

- authorize, issue, sell, offer for sale or solicit offers to buy any shares of our common stock or any convertible securities or any other equity or debt securities or rights to acquire any of our or our subsidiaries' equity or debt securities, subject to certain exceptions, including among other things, the issuance under our stock incentive plan of grants that have been approved by our board of directors (or a board committee) and at least one director appointed by the New Mountain Entities;

- incur indebtedness or refinance any indebtedness, in each case in an amount in excess of a specified threshold;

- hire or replace our chief executive officer; or

- agree or otherwise commit to do any of the foregoing (unless the commitment is conditioned on obtaining the approval of the New Mountain Entities).

These approval rights of the New Mountain Entities will terminate when the New Mountain Entities or certain of their respective assignees beneficially own either (i) less than 50% of the sum of (a) the aggregate number of shares of our common stock that they collectively owned immediately prior to the closing of our IPO and (b) the number of shares of our common stock, if any, acquired following the closing of our IPO (subject to in each case adjustment in the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification or similar changes in our capitalization) or (ii) less than 15% of our common stock outstanding (as set forth on the cover of our then most recently filed annual report on Form 10-K or quarterly report on Form 10-Q). As of June 18, 2018, the New Mountain Entities held approximately 26.3% of our outstanding common stock.

Linde Stockholders Agreement

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

establish any new committee of our board of directors or the board of directors (or equivalent governing body) of any of our subsidiaries, in each case except to the extent prohibited by applicable law or applicable listing exchange rules.

Linde may assign its rights to designate one director for nomination to our board of directors and to designate a director for nomination to the board of directors (or equivalent governing body) of each of our subsidiaries to a person who acquires, in a transaction other than a registered public offering or a sale pursuant to Rule 144 under the Securities Act, at least 50% of the aggregate number of shares of our common stock owned, directly or indirectly, by Linde as of immediately prior to such transaction. As of June 18, 2018, Linde held approximately 9.2% of our outstanding common stock.

Delaware Anti-Takeover Law and Certain Charter and Bylaw Provisions

Delaware Law

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. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a “business combination” with any “interested stockholder” for three years following the date that the person became an interested stockholder, unless either the interested stockholder attained such status with the approval of our board of directors, the business combination is approved by our board of directors and stockholders in a prescribed manner or the interested stockholder acquired at least 85% of our outstanding voting stock in the transaction in which it became an interested stockholder. A “business combination” includes, among other things, a merger or consolidation involving us and the “interested stockholder” and the sale of more than 10% of our assets. In general, an “interested stockholder” is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person. The restrictions contained in Section 203 are not applicable to any of our existing stockholders that owned 15% or more of our outstanding voting stock upon the closing of our IPO.

Staggered Board; Removal of Directors

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

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

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

Our restated certificate of incorporation and our amended and restated bylaws provide that any action required or permitted to be taken by our stockholders at an annual meeting or special meeting of stockholders may only be taken if it is properly brought before such meeting and may not be taken by written action in lieu of a meeting. Our restated

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

Super-Majority Voting

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

Exclusive Forum

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

Registration Rights

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

Demand Registration Rights

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

Form S-3 Registration Rights

In addition, at any time after we become eligible to file a registration statement on Form S-3, subject to specified limitations set forth in the registration rights agreement, either the New Mountain Entities or the holders in the aggregate of 10% or more of our outstanding shares of common stock may demand in writing that we register on Form S-3 all or a portion of the registrable shares so long as the total amount of registrable shares being registered have an aggregate offering price of at least \$10.0 million, unless the registration is of the balance of the registrable

shares held by all the parties to the registration rights agreement.

Incidental Registration Rights

If we propose to file a registration statement under the Securities Act, subject to certain exceptions set forth in the registration rights agreement, the holders of registrable shares will be entitled to notice of the registration and, subject to specified exceptions in the case of an underwritten offering, including market conditions, have the right to require us to register all or a portion of the registrable shares then held by them.

Underwritten Public Offering

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

Expenses and Indemnification

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

Corporate Opportunity

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

Transfer Agent and Registrar

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

Nasdaq Global Market Listing

Our common stock has been publicly traded on the Nasdaq Global Market under the symbol “BLPH” since February 13, 2015.

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the debt securities that we may offer under this prospectus. While the terms we have summarized below will apply generally to any future debt securities we may offer pursuant to this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. If we so indicate in a prospectus supplement, the terms of any debt securities offered under such prospectus supplement may differ from the terms we describe below, and to the extent the terms set forth in a prospectus supplement differ from the terms described below, the terms set forth in the prospectus supplement shall control.

We may sell from time to time, in one or more offerings under this prospectus, debt securities, which may be senior or subordinated. We will issue any such senior debt securities under a senior indenture that we will enter into with a trustee to be named in the senior indenture. We will issue any such subordinated debt securities under a subordinated indenture, which we will enter into with a trustee to be named in the subordinated indenture. We use the term “indentures” to refer to either the senior indenture or the subordinated indenture, as applicable. The indentures will be qualified under the Trust Indenture Act of 1939, as in effect on the date of the indenture. We use the term “debenture trustee” to refer to either the trustee under the senior indenture or the trustee under the subordinated indenture, as applicable.

The following summaries of material provisions of the senior debt securities, the subordinated debt securities and the indentures are subject to, and qualified in their entirety by reference to, all the provisions of the indenture applicable to a particular series of debt securities.

General

Each indenture will provide that debt securities may be issued from time to time in one or more series and may be denominated and payable in foreign currencies or units based on or relating to foreign currencies. Neither indenture will limit the amount of debt securities that may be issued thereunder, and each indenture will provide that the specific terms of any series of debt securities shall be set forth in, or determined pursuant to, an authorizing resolution and/or a supplemental indenture, if any, relating to such series.

We will describe in each prospectus supplement the following terms relating to a series of debt securities:

• the title or designation;

• the aggregate principal amount and any limit on the amount that may be issued;

• the currency or units based on or relating to currencies in which debt securities of such series are denominated and the currency or units in which principal or interest or both will or may be payable;

• whether we will issue the series of debt securities in global form, the terms of any global securities and who the depository will be;

• the maturity date and the date or dates on which principal will be payable;

• the interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the date or dates interest will be payable and the record dates for interest payment dates or the method for determining such dates;

- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- the terms of the subordination of any series of subordinated debt;
- the place or places where payments will be payable;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- the date, if any, after which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional redemption provisions;

the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities;

whether the indenture will restrict our ability to pay dividends, or will require us to maintain any asset ratios or reserves;

whether we will be restricted from incurring any additional indebtedness;

a discussion on any material or special U.S. federal income tax considerations applicable to a series of debt securities;

the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities.

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

Conversion or Exchange Rights

We will set forth in the prospectus supplement the terms, if any, on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities. We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Information Concerning the Debenture Trustee

The debenture trustee, other than during the occurrence and continuance of an event of default under the applicable indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the debenture trustee under such indenture must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the debenture trustee is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check which we will mail to the holder. Unless we otherwise indicate in a prospectus supplement, we will designate the corporate trust office of the debenture trustee in the City of New York as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus

supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the debenture trustee for the payment of the principal of or any premium or interest on any debt securities which remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the security thereafter may look only to us for payment thereof.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

Subordination of Subordinated Debt Securities

Our obligations pursuant to any subordinated debt securities will be unsecured and will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement. The subordinated indenture does not limit the amount of senior indebtedness we may incur. It also does not limit us from issuing any other secured or unsecured debt.

DESCRIPTION OF WARRANTS

General

We may issue warrants to our stockholders to purchase shares of our common stock. We may offer warrants separately or together with one or more debt securities, common stock or rights, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and a bank or trust company, as warrant agent. The warrant agent will act solely as our agent in connection with the certificates relating to the rights of the series of certificates and will not assume any obligation or relationship of agency or trust for or with any holders of rights certificates or beneficial owners of rights. The following description sets forth certain general terms and provisions of the rights to which any prospectus supplement may relate. The particular terms of the warrant to which any prospectus supplement may relate and the extent, if any, to which the general provisions may apply to the rights so offered will be described in the applicable prospectus supplement. To the extent that any particular terms of the warrant, warrant agreement or warrant certificates described in a prospectus supplement differ from any of the terms described below, then the terms described below will be deemed to have been superseded by that prospectus supplement. We encourage you to read the applicable warrant agreement and warrant certificate for additional information before you decide whether to purchase any of our rights.

We will provide in a prospectus supplement the following terms of the warrants being issued:

• the specific designation and aggregate number of, and the price at which we will issue, the warrants;

• the currency or currency units in which the offering price, if any, and the exercise price are payable;

• the designation, amount and terms of the securities purchasable upon exercise of the warrants;

• if applicable, the exercise price for shares of our common stock and the number of shares of common stock to be received upon exercise of the warrants;

• if applicable, the exercise price for shares of our preferred stock, the number of shares of preferred stock to be received upon exercise, and a description of that series of our preferred stock;

• if applicable, the exercise price for our debt securities, the amount of debt securities to be received upon exercise, and a description of that series of debt securities;

• the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;

• whether the warrants will be issued in fully registered form or bearer form, in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;

• any applicable material U.S. federal income tax consequences;

• the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;

the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;

if applicable, the date from and after which the warrants and the common stock, preferred stock and/or debt securities will be separately transferable;

if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;

information with respect to book-entry procedures, if any;

the anti-dilution provisions of the warrants, if any;

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any redemption or call provisions;

whether the warrants may be sold separately or with other securities as parts of units; and

any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

Each warrant will entitle the holder of rights to purchase for cash the principal amount of shares of common stock or other securities at the exercise price provided in the applicable prospectus supplement. Warrants may be exercised at any time up to the close of business on the expiration date for the rights provided in the applicable prospectus supplement.

Holders may exercise warrants as described in the applicable prospectus supplement. Upon receipt of payment and the warrant certificate properly completed and duly executed at the corporate trust office of the rights agent or any other office indicated in the prospectus supplement, we will, as soon as practicable, forward the shares of common stock or other securities, as applicable, purchasable upon exercise of the rights. If less than all of the warrants issued in any rights offering are exercised, we may offer any unsubscribed securities directly to persons other than stockholders, to or through agents, underwriters or dealers or through a combination of such methods, including pursuant to standby arrangements, as described in the applicable prospectus supplement.

Warrant Agent

The warrant agent for any warrants we offer will be set forth in the applicable prospectus supplement.

DESCRIPTION OF RIGHTS

General

We may issue rights to our stockholders to purchase shares of our common stock or the other securities described in this prospectus. We may offer rights separately or together with one or more additional rights, debt securities, common stock or warrants, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. Each series of rights will be issued under a separate rights agreement to be entered into between us and a bank or trust company, as rights agent. The rights agent will act solely as our agent in connection with the certificates relating to the rights of the series of certificates and will not assume any obligation or relationship of agency or trust for or with any holders of rights certificates or beneficial owners of rights. The following description sets forth certain general terms and provisions of the rights to which any prospectus supplement may relate. The particular terms of the rights to which any prospectus supplement may relate and the extent, if any, to which the general provisions may apply to the rights so offered will be described in the applicable prospectus supplement. To the extent that any particular terms of the rights, rights agreement or rights certificates described in a prospectus supplement differ from any of the terms described below, then the terms described below will be deemed to have been superseded by that prospectus supplement. We encourage you to read the applicable rights agreement and rights certificate for additional information before you decide whether to purchase any of our rights.

We will provide in a prospectus supplement the following terms of the rights being issued:

- the date of determining the stockholders entitled to the rights distribution;
- the aggregate number of shares of common stock or other securities purchasable upon exercise of the rights;
- the exercise price;
- the aggregate number of rights issued;
- whether the rights are transferrable and the date, if any, on and after which the rights may be separately transferred;
- the date on which the right to exercise the rights will commence, and the date on which the right to exercise the rights will expire;
- the method by which holders of rights will be entitled to exercise;
- the conditions to the completion of the offering, if any;
- the withdrawal, termination and cancellation rights, if any;
- whether there are any backstop or standby purchaser or purchasers and the terms of their commitment, if any;
- whether stockholders are entitled to oversubscription rights, if any;
- any applicable U.S. federal income tax considerations; and
- any other terms of the rights, including terms, procedures and limitations relating to the distribution, exchange and exercise of the rights, as applicable.

Each right will entitle the holder of rights to purchase for cash the principal amount of shares of common stock or other securities at the exercise price provided in the applicable prospectus supplement. Rights may be exercised at any time up to the close of business on the expiration date for the rights provided in the applicable prospectus supplement.

Holders may exercise rights as described in the applicable prospectus supplement. Upon receipt of payment and the rights certificate properly completed and duly executed at the corporate trust office of the rights agent or any other office indicated in the prospectus supplement, we will, as soon as practicable, forward the shares of common stock or other securities, as applicable, purchasable upon exercise of the rights. If less than all of the rights issued in any rights offering are exercised, we may offer any unsubscribed securities directly to persons other than stockholders, to or through agents, underwriters or dealers

or through a combination of such methods, including pursuant to standby arrangements, as described in the applicable prospectus supplement.

Rights Agent

The rights agent for any rights we offer will be set forth in the applicable prospectus supplement.

DESCRIPTION OF UNITS

The following description, together with the additional information that we include in any applicable prospectus supplements summarizes the material terms and provisions of the units that we may offer under this prospectus. While the terms we have summarized below will apply generally to any units that we may offer under this prospectus, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement. The terms of any units offered under a prospectus supplement may differ from the terms described below.

We will incorporate by reference from reports that we file with the SEC, the form of unit agreement that describes the terms of the series of units we are offering, and any supplemental agreements, before the issuance of the related series of units. The following summaries of material terms and provisions of the units are subject to, and qualified in their entirety by reference to, all the provisions of the unit agreement and any supplemental agreements applicable to a particular series of units. We urge you to read the applicable prospectus supplements related to the particular series of units that we may offer under this prospectus, as well as any related free writing prospectuses and the complete unit agreement and any supplemental agreements that contain the terms of the units.

General

We may issue units consisting of common stock, one or more debt securities, warrants or rights for the purchase of common stock and/or debt securities in one or more series, in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each security included in the unit. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

We will describe in the applicable prospectus supplement the terms of the series of units being offered, including:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;

- any provisions of the governing unit agreement that differ from those described below; and

- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The provisions described in this section, as well as those set forth in any prospectus supplement or as described under “Description of Capital Stock,” “Description of Debt Securities,” “Description of Warrants” and “Description of Rights” will apply to each unit, as applicable, and to any common stock, debt security, warrant or right included in each unit, as applicable.

Unit Agent

The name and address of the unit agent for any units we offer will be set forth in the applicable prospectus supplement.

Issuance in Series

We may issue units in such amounts and in such numerous distinct series as we determine.

Enforceability of Rights by Holders of Units

Each unit agent will act solely as our agent under the applicable unit agreement and will not assume any obligation or relationship of agency or trust with any holder of any unit. A single bank or trust company may act as unit agent for more than one series of units. A unit agent will have no duty or responsibility in case of any default by us under the applicable unit agreement or unit, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a unit may, without the consent of the related unit agent or the holder of any other unit, enforce by appropriate legal action its rights as holder under any security included in the unit.

Provisions of Delaware Law Governing Business Combinations

We are subject to the “business combination” provisions of Section 203 of the DGCL. In general, such provisions prohibit a publicly held Delaware corporation from engaging in any “business combination” transactions with any “interested stockholder” for a period of three years after the date on which the person became an “interested stockholder,” unless:

prior to such date, the board of directors approved either the “business combination” or the transaction which resulted in the “interested stockholder” obtaining such status; or

upon consummation of the transaction which resulted in the stockholder becoming an “interested stockholder,” the “interested stockholder” owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding (but not the outstanding voting stock owned by the “interested stockholder”) those shares owned by (a) persons who are directors and also officers and (b) employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

at or subsequent to such time the “business combination” is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock which is not owned by the “interested stockholder.”

A “business combination” is defined to include mergers, asset sales and other transactions resulting in financial benefit to a stockholder. In general, an “interested stockholder” is a person who, together with affiliates and associates, owns 15% or more of a corporation’s voting stock or within three years did own 15% or more of a corporation’s voting stock. The statute could prohibit or delay mergers or other takeover or change in control attempts with respect to us and, accordingly, may discourage attempts to acquire us.

Limitations on Liability and Indemnification of Officers and Directors

Section 145 of the DGCL authorizes a court to award, or a corporation’s board of directors to grant, indemnity to directors and officers in terms sufficiently broad to permit such indemnification under certain circumstances for liabilities (including reimbursement for expenses incurred) arising under the Securities Act of 1933. Our amended and restated certificate of incorporation limits the liability of our officers and directors to the fullest extent permitted by the DGCL, and our amended and restated certificate of incorporation provides that we will indemnify our officers and directors to the fullest extent permitted by such law.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers or persons controlling the registrant pursuant to the foregoing provisions, the registrant has been informed that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

LEGAL MATTERS

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., New York, New York, will pass upon the validity of the issuance of the securities to be offered by this prospectus.

EXPERTS

The consolidated financial statements of Bellerophon Therapeutics, Inc. (formerly Bellerophon Therapeutics LLC) as of December 31, 2017 and 2016, and for each of the years in the three-year period ended December 31, 2017, have been incorporated by reference herein in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, and file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy these reports, proxy statements and other information at the SEC's public reference facilities at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference facilities. SEC filings are also available at the SEC's web site at <http://www.sec.gov>.

This prospectus is only part of a registration statement on Form S-3 that we have filed with the SEC under the Securities Act and therefore omits certain information contained in the registration statement. We have also filed exhibits and schedules with the registration statement that are excluded from this prospectus, and you should refer to the applicable exhibit or schedule for a complete description of any statement referring to any contract or other document. You may inspect a copy of the registration statement, including the exhibits and schedules, without charge, at the public reference room or obtain a copy from the SEC upon payment of the fees prescribed by the SEC.

We also maintain a website at www.bellerophon.com, through which you can access our SEC filings. The information set forth on, or accessible from, our website is not part of this prospectus.

INCORPORATION OF INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information that we file with them. Incorporation by reference allows us to disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. This prospectus omits certain information contained in the registration statement, as permitted by the SEC. You should refer to the registration statement and any prospectus supplement filed hereafter, including the exhibits, for further information about us and the securities we may offer pursuant to this prospectus. Statements in this prospectus regarding the provisions of certain documents filed with, or incorporated by reference in, the registration statement are not necessarily complete and each statement is qualified in all respects by that reference. Copies of all or any part of the registration statement, including the documents incorporated by reference or the exhibits, may be obtained upon payment of the prescribed rates at the offices of the SEC listed above in "Where You Can Find More Information." The documents we are incorporating by reference are:

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our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, filed on March 15, 2018, as amended on May 17, 2018;

our Quarterly Report on Form 10-Q for the period ended March 31, 2018, filed on May 10, 2018;

our Current Reports on Form 8-K filed on January 17, 2018, March 26, 2018, April 26, 2018 and May 24, 2018;

the description of our common stock contained in our Registration Statement on Form 8-A, filed on February 10, 2015, pursuant to Section 12(b) of the Exchange Act, which incorporates by reference the description of the shares of our common stock contained in our Registration Statement on Form S-1 (File No. 333-201474) filed on January 13, 2015, as amended on February 3, 2015, and declared effective by the SEC on February 13, 2015 and any amendment or report filed with the SEC for purposes of updating such description; and

all reports and other documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act after the date of this prospectus and prior to the termination or completion of the offering of securities under this prospectus shall be deemed to be incorporated by reference in this prospectus and to be a part hereof from the date of filing such reports and other documents.

Unless otherwise noted, the SEC file number for each of the documents listed above is 001-36845.

In addition, all reports and other documents filed by us pursuant to the Exchange Act after the date of the initial registration statement and prior to effectiveness of the registration statement shall be deemed to be incorporated by reference into this prospectus.

Any statement contained in this prospectus or in a document incorporated or deemed to be incorporated by reference into this prospectus will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or any other subsequently filed document that is deemed to be incorporated by reference into this prospectus modifies or supersedes the statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

You may request, orally or in writing, a copy of any or all of the documents incorporated herein by reference. These documents will be provided to you at no cost, by contacting: Investor Relations, Bellerophon Therapeutics, Inc., 184 Liberty Corner Road, Suite 302, or call (908) 574-4770.

You should rely only on information contained in, or incorporated by reference into, this prospectus and any prospectus supplement. We have not authorized anyone to provide you with information different from that contained in this prospectus or incorporated by reference in this prospectus. We are not making offers to sell the securities in any jurisdiction in which such an offer or solicitation is not authorized or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make such offer or solicitation.

Shares of Common Stock

PROSPECTUS SUPPLEMENT

H.C. Wainwright & Co.

, 2019

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