

PUMA BIOTECHNOLOGY, INC.

Form S-3

January 29, 2014

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As filed with the Securities and Exchange Commission on January 29, 2014

Registration No. 333-

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

FORM S-3
REGISTRATION STATEMENT

Under
The Securities Act of 1933

Puma Biotechnology, Inc.

(Exact name of Registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

77-0683487
(I.R.S. Employer
Identification No.)

10880 Wilshire Boulevard, Suite 2150

Los Angeles, California 90024

(424) 248-6500

(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

Alan H. Auerbach

President and Chief Executive Officer

Puma Biotechnology, Inc.

10880 Wilshire Boulevard, Suite 2150

Los Angeles, California 90024

(424) 248-6500

(Name, address, including zip code, and telephone number, including area code, of agent for service)

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Approximate date of commencement of proposed sale to the public: Promptly after the effective date of this Registration Statement.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

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

Large accelerated filer Accelerated Filer
 Non-accelerated filer (Do not check if a smaller reporting company) Smaller Reporting Company

CALCULATION OF REGISTRATION FEE

| Title of Each Class of Securities to be Registered | Proposed | Amount of Registration Fee |
|--|---|----------------------------|
| | Maximum Aggregate Offering Price (1)(2) | |
| | | |

| | | |
|--|---------------|----------|
| Common Stock, par value \$0.0001 per share | \$115,000,000 | \$14,812 |
|--|---------------|----------|

- (1) Estimated solely for the purpose of computing the amount of the registration fee pursuant to Rule 457(o) under the Securities Act.
- (2) Includes shares subject to the underwriters' option to purchase additional shares.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until this registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to Completion

Preliminary Prospectus dated January 29, 2014

PROSPECTUS

Shares

Puma Biotechnology, Inc.

Common Stock

We are selling _____ shares of our common stock.

Our shares trade on the New York Stock Exchange under the symbol **PBYI**. On January 28, 2014, the last sale price of the shares as reported on the New York Stock Exchange was \$125.18 per share.

Investing in the common stock involves risks that are described in the Risk Factors section beginning on page 7 of this prospectus.

| | Per Share | Total |
|--------------------------------------|------------------|--------------|
| Public offering price | \$ | \$ |
| Underwriting discount ⁽¹⁾ | \$ | \$ |
| Proceeds, before expenses, to us | \$ | \$ |

(1) See Underwriting for additional disclosure regarding underwriting discounts, commissions and estimated offering expenses.

The underwriters may also exercise their option to purchase up to an additional _____ shares from us, at the public offering price, less the underwriting discount, for 30 days after the date of this prospectus.

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 shares will be ready for delivery on or about _____, 2014.

BofA Merrill Lynch

Citigroup
The date of this prospectus is _____, 2014.

Leerink Partners

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Neither we nor the underwriters have authorized anyone to provide any information other than that contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the underwriters are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus is accurate only as of the date on the front cover of this prospectus, regardless of the time of delivery of this prospectus or any sale of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

For investors outside of the United States: Neither we nor the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than the United States. Persons outside of the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside of the United States.

This prospectus includes estimates, statistics and other industry and market data that we obtained from industry publications, research, surveys and studies conducted by third parties and publicly available information. Such data involves a number of assumptions and limitations and contains projections and estimates of the future performance of the industries in which we operate that are subject to a high degree of uncertainty. This prospectus also includes data based on our own internal estimates. We caution you not to give undue weight to such projections, assumptions and estimates.

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PROSPECTUS SUMMARY

*The following summary highlights selected information contained elsewhere or incorporated by reference in this prospectus. This summary is not complete and does not contain all of the information that should be considered before investing in our common stock. Before making an investment decision, investors should carefully read the entire prospectus, including the information incorporated by reference in this prospectus, paying particular attention to the risks referred to under the headings *Cautionary Statement Regarding Forward-Looking Statements*, *Risk Factors* and our financial statements and the notes to those financial statements. As used in this prospectus, unless the context requires otherwise, the terms *Company*, *we*, *our* and *us* refer to Puma Biotechnology, Inc., a Delaware corporation formed on April 27, 2007 and formerly known as Innovative Acquisitions Corp., together with its wholly-owned subsidiary, Puma Biotechnology Ltd, and the term *Former Puma* refers to Puma Biotechnology, Inc., a private Delaware corporation that merged with and into us in October 2011.*

Our Company

We are a development-stage biopharmaceutical company with a focus on the acquisition, development and commercialization of innovative products to enhance cancer care. We aim to acquire proprietary rights to these products, by license or otherwise, fund their research and development and bring the products to market. Our efforts and resources to date have been focused primarily on acquiring and developing our pharmaceutical technologies, raising capital and recruiting personnel.

We currently license the rights to three drug candidates:

PB272 (neratinib (oral)), which we are developing for the treatment of advanced breast cancer patients, non-small cell lung cancer patients and patients with HER2 mutation-positive solid tumors;

PB272 (neratinib (intravenous)), which we are developing for the treatment of advanced cancer patients; and

PB357, which we believe can serve as a backup compound to PB272, and which we are evaluating for further development.

We are initially focused on developing neratinib for the treatment of patients with human epidermal growth factor receptor type 2, or HER2, positive breast cancer, HER2 mutated non-small cell lung cancer, HER2-negative breast cancer that has a HER2 mutation and other solid tumors that have an activating mutation in HER2. Studies show that approximately 20% to 25% of breast cancer tumors have an over-expression of the HER2 protein. Women with breast cancer that over-expresses HER2, referred to as HER2-positive breast cancer, are at greater risk for disease progression and death than women whose tumors do not over-express HER2. Therapeutic strategies, such as the use of Herceptin (trastuzumab), Perjeta (pertuzumab), and Kadcyca (T-DM1), produced by Genentech, and Tykerb (lapatinib), produced by GlaxoSmithKline, given either alone or in combination with chemotherapy, have been developed to improve the treatment of this cancer by binding HER2. Based on pre-clinical and clinical studies to date, we believe that neratinib may offer an advantage over existing treatments by more potently inhibiting HER2 at a different site and using a different mechanism than these other drugs.

Currently, the first-line therapy approved by the U.S. Food and Drug Administration, or FDA, for treatment of HER2-positive metastatic breast cancer is the combination of Perjeta plus Herceptin and taxane chemotherapy. The

drug Tykerb, given in combination with the chemotherapy drug capecitabine, is also FDA approved for the treatment of HER2-positive metastatic breast cancer that has failed prior treatment. In a Phase III clinical trial, patients with HER2-positive metastatic breast cancer who received the combination of Tykerb plus capecitabine demonstrated a median progression free survival, or PFS, of 27.1 weeks and a response rate of 23.7%.

Results from a Phase II clinical study, where patients with HER2-positive metastatic breast cancer who had failed prior treatments were administered the combination of neratinib and capecitabine, demonstrated a median PFS of 40.3 weeks and an overall response rate of 64%. In February 2013, we announced that we had reached an agreement with the FDA under a Special Protocol Assessment, or SPA, for our planned Phase III clinical trial of PB272 in patients with HER2-positive metastatic breast cancer who have failed two or more prior treatments

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(third-line disease). The European Medicines Agency, or EMA, has also provided follow-on scientific advice, or SA, consistent with that of the FDA regarding our Phase III trial design and endpoints to be used and ability of such design to support the submission of a European Union, or EU, Market Authorization Application, or MAA. We commenced our Phase III clinical trial of neratinib (oral) for breast cancer patients who have previously failed two or more prior HER2-directed treatments in the second quarter of 2013.

The Phase III trial is a randomized trial of PB272 plus Xeloda versus Tykerb plus Xeloda in patients with third-line HER2-positive metastatic breast cancer. The trial is expected to enroll approximately 600 patients who will be randomized (1:1) to receive either PB272 plus Xeloda or Tykerb plus Xeloda. The trial will be conducted at approximately 150 sites in North America, Europe and Asia-Pacific. The co-primary endpoints of the trial are progression free survival and overall survival. We plan to use the progression free survival data from the trial as the basis for submission of a New Drug Application, or NDA, to the FDA for accelerated approval of PB272 for this indication. We also plan to use the progression free survival data from this trial to support a MAA to the EMA for conditional approval for PB272 in the same indication.

We are also exploring the safety and efficacy of neratinib (oral):

in combination with tamsirolimus in patients with HER2-positive metastatic breast cancer who have failed multiple prior treatments;

for the treatment of patients with HER2-positive metastatic breast cancer with brain metastases;

for the treatment of HER2-positive neoadjuvant breast cancer;

for the adjuvant treatment of HER2-positive breast cancer in patients who have completed adjuvant treatment with Herceptin;

for the treatment of patients with first line HER2-positive metastatic breast cancer who have not previously received treatment in the metastatic setting;

for the treatment of HER2 mutated non-small cell lung cancer;

for the treatment of patients with HER2-negative breast cancer that has a HER2 mutation; and

for the treatment of patients with solid tumors who have an activating HER2 mutation.

We have on-going Phase II clinical trials for each of these indications.

We licensed the exclusive worldwide rights to our current drug candidates from Pfizer Inc., or Pfizer, which had previously been responsible for the clinical trials regarding neratinib. We have modified Pfizer's clinical development

strategy and during the next 12 to 18 months plan to:

continue our Phase III clinical trials of neratinib in patients with HER2-positive metastatic breast cancer who have previously failed two or more prior treatments;

commence a Phase III trial of neratinib for the neoadjuvant treatment of HER2-positive breast cancer and for the neoadjuvant treatment of a subset of patients with HER2-negative breast cancer;

continue the on-going Phase II clinical trials of neratinib in the neoadjuvant treatment of HER2-positive breast cancer, the ongoing Phase II trial in patients with HER2-positive metastatic breast cancer that has metastasized to the brain, the ongoing Phase II trial in the treatment of HER2 mutated non-small cell lung cancer, the ongoing Phase II trial in the treatment of patients with HER2-negative breast cancer that have a HER2 mutation, the ongoing Phase II trial in the treatment of solid tumors that have an activating HER2 mutation, the ongoing Phase III trial for the adjuvant treatment of HER2 positive breast cancer in patients who have completed adjuvant treatment with Herceptin, and the ongoing Phase II trial for the treatment of patients with first line HER2-positive metastatic breast cancer who have not previously received treatment in the metastatic setting; and

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continue to evaluate the application of neratinib in the treatment of other forms of HER2-positive or HER2 mutated cancers where there may be unmet medical needs.

Recent Developments

In December 2013, we announced top line results from the Phase II clinical trial of neratinib for the neoadjuvant treatment of breast cancer, referred to as the I-SPY 2 TRIAL. The I-SPY 2 TRIAL, or Investigation of Serial Studies to Predict Your Therapeutic Response with Imaging And moLecular Analysis 2, is a randomized Phase II clinical trial for women with newly diagnosed Stage 2 or higher (tumor size at least 2.5 cm) breast cancer that addresses whether adding investigational drugs to standard chemotherapy in the neoadjuvant setting is better than standard chemotherapy. The primary endpoint is pathological complete response, or pCR, in the breast and the lymph nodes at the time of surgery. The goal of the trial is to match investigational regimens with patient subsets on the basis of molecular characteristics, referred to as biomarker signatures, that benefit from the regimen.

The I-SPY 2 TRIAL involves an adaptive trial design based on Bayesian predictive probability that a regimen will be shown to be statistically superior to standard therapy in an equally randomized 300-patient confirmatory trial. Regimens that have a high Bayesian predictive probability of showing superiority in at least one of 10 predefined signatures graduate from the trial. Regimens are dropped for futility if they show a low predictive probability of showing superiority over standard therapy in all 10 signatures. A maximum total of 120 patients can be assigned to each experimental regimen. A regimen can graduate early and at any time after having 60 patients assigned to it. The neratinib-containing regimen, which was neratinib plus paclitaxel followed by doxorubicin and cyclophosphamide, graduated from the I-SPY 2 TRIAL based on having a high probability of success in Phase III with a signature of HER2-positive/HR-negative. In this group, treatment with the neratinib-containing regimen resulted in a higher pCR rate compared to the control arm, which was standard neoadjuvant chemotherapy: paclitaxel in combination with Herceptin (trastuzumab) followed by doxorubicin and cyclophosphamide. The Bayesian probability of superiority for the neratinib-containing regimen compared to standard therapy is 94.7%, which is analogous to a p-value of 0.053. In addition, the Bayesian predictive probability of showing statistical superiority in a 300-patient Phase III randomized trial of paclitaxel plus neratinib versus paclitaxel plus trastuzumab, both followed by doxorubicin/cyclophosphamide, is 78.1%.

There were 115 patients assigned to neratinib in the trial, including 65 patients who were HER2-positive. For the patients in the trial who were HER2-positive, including those who were either hormone receptor-positive or negative, treatment with the neratinib-containing regimen also resulted in a higher pCR rate compared to the control arm. The Bayesian probability of superiority for the neratinib-containing regimen is 95.3%, which is analogous to a p-value of 0.047. In addition, the Bayesian predictive probability of showing statistical superiority in a 300-patient Phase III randomized trial of paclitaxel plus neratinib versus paclitaxel plus trastuzumab is 72.5%. Based on the results from the I-SPY 2 TRIAL, neratinib is now eligible for the upcoming I-SPY 3 Phase III trial. We intend to provide additional detail regarding the results of the I-SPY 2 TRIAL for PB272 at a future scientific meeting.

Risks Affecting Us

Our business is subject to numerous risks, as more fully described in the section of this prospectus entitled "Risk Factors," including the following:

We currently have no product revenues and no products approved for marketing, and will need to raise additional capital to operate our business.

We have a limited operating history and are not profitable and may never become profitable.

We are heavily dependent on the success of neratinib (oral), our lead drug candidate, which is still under clinical development, and we cannot be certain that neratinib (oral) will receive regulatory approval or be successfully commercialized even if we receive regulatory approval.

Clinical trials are very expensive, time-consuming and difficult to design and implement.

The results of our clinical trials may not support our drug candidate claims.

We depend significantly on intellectual property licensed from Pfizer and the termination of this license would significantly harm our business and future prospects.

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Our ability to commercialize our potential products will depend on our ability to sell such products without infringing the patent or proprietary rights of third parties. If we are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in any such litigation would have a material adverse effect on our business.

Corporate Information

We were incorporated on April 27, 2007 in Delaware under the name Innovative Acquisitions Corp. Until October 4, 2011, we were a shell company with nominal assets and no operations. On September 29, 2011, we entered into an Agreement and Plan of Merger with IAC Merger Corporation, a Delaware corporation and our wholly-owned subsidiary, or Merger Sub, and Former Puma. On October 4, 2011, Merger Sub merged with and into Former Puma, and Former Puma, as the surviving entity, became our wholly-owned subsidiary. In this prospectus, we refer to the merger between Merger Sub and Former Puma as the Merger. In November 2012, we established and incorporated Puma Biotechnology Ltd, a wholly owned subsidiary, for the sole purpose of serving as our legal representative in the United Kingdom and the European Union in connection with our clinical trial activity in those countries.

Our principal executive offices are located at 10880 Wilshire Boulevard, Suite 2150, Los Angeles, California 90024. Our telephone number is (424) 248-6500. Our website is www.pumabiotechnology.com. Information contained on our website is not incorporated by reference into, and should not be considered a part of, this prospectus.

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THE OFFERING

| | |
|---|--|
| Common Stock Offered by Us | shares |
| Common Stock Outstanding After this Offering | shares |
| Option to Purchase Additional Shares | The underwriters have a 30-day option to purchase up to an additional shares of our common stock at the public offering price less the underwriting discounts and commissions. |
| Use of Proceeds | We intend to use the net proceeds of this offering for the overall development of our drug candidates, including, but not limited to, research and development and clinical trial expenditures, and for general corporate and working capital purposes. See Use of Proceeds. |
| Assumed Public Offering Price | \$ |
| Risk Factors | You should read the Risk Factors section beginning on page 7 of this prospectus for a discussion of factors to consider before deciding to invest in shares of our common stock. |
| New York Stock Exchange Symbol | PBYI |
| Unless otherwise noted, the number of shares of our common stock outstanding prior to and after this offering is based on 28,689,304 shares outstanding as of September 30, 2013, and excludes: | |

2,373,309 shares of common stock issuable upon the exercise of options outstanding as of September 30, 2013 at a weighted average exercise price of \$14.76 per share;

1,143,465 shares of common stock reserved for future issuance under our incentive award plan; and

2,116,250 shares of our common stock issuable upon the exercise of a warrant held by Alan Auerbach, our President and Chief Executive Officer, at \$16.00 per share.

Unless otherwise indicated, the information in this prospectus assumes no exercise by the underwriters of their option to purchase additional shares of common stock from us.

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The following tables set forth a summary of our historical financial data as of, and for the periods ended on, the dates indicated. The statement of operations data for the period from September 15, 2010 (inception) to December 31, 2010 and the years ended December 31, 2011 and 2012 is derived from our audited financial statements incorporated by reference in this prospectus. The statement of operations data for the nine months ended September 30, 2012 and 2013 and for the period from September 15, 2010 (inception) to September 30, 2013 and the balance sheet data as of September 30, 2013 have been derived from our unaudited financial statements incorporated by reference in this prospectus. You should read this data together with Management's Discussion and Analysis of Financial Condition and Results of Operations and our audited financial statements and related notes incorporated by reference in this prospectus. Our historical results are not necessarily indicative of results to be expected in any future period, and our results for any interim period are not necessarily indicative of results to be expected for a full fiscal year.

| (in thousands except share and per share data) | Period from September 15, 2010 (date of inception) to December 31, 2010 | Year ended December 31, 2011 | Year ended December 31, 2012 | Nine Months Ended September 30, 2012 | September 30, 2013 | Period from September 15, 2010 (date of inception) to September 30, 2013 |
|--|---|---------------------------------------|---------------------------------------|--|-----------------------|---|
| Operating expenses: | | | | | | |
| General and administrative | \$ 7 | \$ 9,331 | \$ 24,814 | \$ 11,149 | \$ 6,804 | \$ 40,956 |
| Research and development | | 826 | 49,636 | 41,354 | 32,040 | 82,502 |
| Totals | 7 | 10,157 | 74,450 | 52,503 | 38,844 | 123,458 |
| Loss from operations | (7) | (10,157) | (74,450) | (52,503) | (38,844) | (123,458) |
| Other income (expenses): | | | | | | |
| Interest income | | 4 | 98 | 63 | 128 | 230 |
| Other income (expense) | | (80) | | | 3 | (77) |
| Totals | | (76) | 98 | 63 | 131 | 153 |
| Net loss | \$ (7) | \$ (10,233) | \$ (74,352) | \$ (52,440) | \$ (38,713) | \$ (123,305) |
| Net loss per common share basic and diluted | \$ (0.002) | \$ (1.321) | \$ (3.422) | \$ (2.617) | \$ (1.350) | |
| Weighted-average common shares outstanding basic and diluted | 4,000,000 | 7,746,529 | 21,725,986 | 20,040,000 | 28,678,439 | |

(1)

Please see Note 2 to our audited financial statements for the year ended December 31, 2012 and Note 2 to our unaudited financial statements for the nine months ended September 30, 2013 incorporated by reference in this prospectus for an explanation of the method used to calculate basic and diluted net loss per share of common stock.

| Balance sheet data (in thousands) | As of September 30, 2013 | |
|--|---------------------------------|-----------------------|
| | Actual | As Adjusted(1) |
| Cash and cash equivalents | \$ 51,261 | \$ |
| Marketable securities | 44,377 | |
| Total Assets | 115,109 | |
| Total Liabilities | 20,349 | |
| Deficit accumulated during the development stage | (123,305) | |
| Total stockholders' equity | 94,760 | |

- (1) Reflects the sale by us of an assumed shares of our common stock in this offering at an assumed public offering price of \$ per share, the last reported sale price of our common stock on , 2014, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each \$1.00 increase (decrease) in the assumed public offering price, would increase (decrease) each of cash and cash equivalents, total assets and total stockholders' equity by approximately \$ million, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, assuming that the number of shares offered by us, as set forth above, remains the same. Each increase (decrease) of 100,000 shares in the number of shares offered by us at the assumed public offering price would increase (decrease) each of cash and cash equivalents, total assets and total stockholders' equity by approximately \$ million. The as adjusted information discussed above is illustrative only and will be adjusted based on the actual public offering price.

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RISK FACTORS

Investing in our common stock involves a high degree of risk. In addition to the other information set forth in this prospectus, you should carefully consider the factors discussed below when considering an investment in our common stock. If any of the events contemplated by the following discussion of risks should occur, our business, results of operations and financial condition could suffer significantly. As a result, you could lose some or all of your investment in our common stock. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business.

Risks Related to our Business

We currently have no product revenues and no products approved for marketing, and will need to raise additional capital to operate our business.

To date, we have generated no product revenues. Until, and unless, we receive approval from the U.S. Food and Drug Administration, or FDA, and other regulatory authorities overseas for one or more of our drug candidates, we cannot market or sell our products and will not have product revenues. Currently, our only drug candidates are neratinib (oral), neratinib (intravenous) and PB357, and none of these products has been approved by the FDA for sale in the United States or by other regulatory authorities for sale outside the United States. Moreover, each of these drug candidates is in clinical development and will require significant time and capital before we can even apply for approval from the FDA. Therefore, for the foreseeable future, we do not expect to achieve any product revenues and will have to fund all of our operations and capital expenditures from cash on hand, licensing fees and grants, and potentially, future offerings of our securities. We believe that our cash on hand is sufficient to fund our operations into the first half of 2015. However, changes may occur that would consume our available capital faster than anticipated, including changes in and progress of our development activities, acquisitions of additional drug candidates and changes in regulation. In such situations, we may need to seek additional sources of financing, which may not be available on favorable terms, if at all. If we do not succeed in timely raising additional funds on acceptable terms, we may be unable to complete planned pre-clinical and clinical trials or obtain approval of any drug candidates from the FDA and other regulatory authorities. In addition, we could be forced to discontinue product development and forego attractive business opportunities. Any additional sources of financing will likely involve the issuance of additional equity securities, which will have a dilutive effect on our stockholders.

We have a limited operating history and are not profitable and may never become profitable.

We were formed in April 2007 and were a shell company with no specific business plan or purpose until we acquired Former Puma on October 4, 2011. Former Puma was a development stage company formed in September 2010 and, prior to entering into the license agreement with Pfizer in August 2011, its operations were limited to identifying compounds for in-licensing. As a result, we have a history of operating losses and no meaningful operations upon which to evaluate our business. We expect to incur substantial losses and negative operating cash flow for the foreseeable future as we continue development of our drug candidates, which we do not expect will be commercially available for a number of years, if at all. Even if we succeed in developing and commercializing one or more drug candidates, we expect to incur substantial losses for the foreseeable future and may never become profitable. The successful development and commercialization of any drug candidates will require us to perform a variety of functions, including:

undertaking pre-clinical development and clinical trials;

hiring additional personnel;

participating in regulatory approval processes;

formulating and manufacturing products;

initiating and conducting sales and marketing activities; and

implementing additional internal systems and infrastructure.

We will likely need to raise additional capital in order to fund our business and generate significant revenue in order to achieve and maintain profitability. We may not be able to generate this revenue, raise additional capital or achieve profitability in the future. Our failure to achieve or maintain profitability could negatively impact the value of our common stock.

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We are heavily dependent on the success of neratinib (oral), our lead drug candidate, which is still under clinical development, and we cannot be certain that neratinib (oral) will receive regulatory approval or be successfully commercialized even if we receive regulatory approval.

We currently have no products that are approved for commercial sale, and we may never be able to develop marketable drug products. We expect that a substantial portion of our efforts and expenditures over the next few years will be devoted to our lead drug candidate, neratinib (oral). Accordingly, our business currently depends heavily on the successful development, regulatory approval and commercialization of neratinib (oral). We cannot be certain that neratinib (oral) will receive regulatory approval or be successfully commercialized even if we receive regulatory approval. The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of drug products are and will remain subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries that each have differing regulations. We are not permitted to market neratinib (oral) or any of our drug candidates in the United States until they receive approval of a New Drug Application, or NDA, from the FDA, or in any foreign countries until they receive the requisite approval from such countries. We have not submitted an NDA to the FDA or comparable applications to other regulatory authorities and do not expect to be in a position to do so for the foreseeable future. Obtaining approval of an NDA is an extensive, lengthy, expensive and inherently uncertain process, and the FDA may delay, limit or deny approval of neratinib (oral) for many reasons, including:

we may not be able to demonstrate that neratinib (oral) is safe and effective as a treatment for our targeted indications to the satisfaction of the FDA;

the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA for marketing approval;

the FDA may disagree with the number, design, size, conduct or implementation of our clinical trials;

the clinical research organization that we retain to conduct clinical trials or any other third parties involved in the conduct of the trials may take actions outside of our control that materially adversely impact our clinical trials;

the FDA may not find the data from pre-clinical studies and clinical trials sufficient to demonstrate that the clinical and other benefits of neratinib (oral) outweigh its risks;

the FDA may disagree with our interpretation of data from our pre-clinical studies and clinical trials or may require that we conduct additional studies;

the FDA may not accept data generated at one or more of our clinical study sites;

if our NDA is reviewed by an advisory committee, the FDA may have difficulties scheduling an advisory committee meeting in a timely manner or the advisory committee may recommend against approval of our application or may recommend that the FDA require, as a condition of approval, additional pre-clinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions;

the advisory committee may recommend that the FDA require, as a condition of approval, additional pre-clinical studies or clinical studies, limitations on approved labeling or distribution and use restrictions;

the FDA may require development of a Risk Evaluation and Mitigation Strategy as a condition to approval;

the FDA may identify deficiencies in the manufacturing processes or facilities of our third-party manufacturers; or

the FDA may change its approval policies or adopt new regulations.

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Clinical trials are very expensive, time-consuming and difficult to design and implement.

Each of our drug candidates is still in development and will require extensive clinical testing before we can submit an NDA for regulatory approval. We cannot predict with any certainty if or when we might submit an NDA for regulatory approval for any of our drug candidates or whether any such NDA will be approved by the FDA. Human clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. The clinical trial process is also time-consuming. We estimate that clinical trials of our drug candidates will take at least several years to complete. Furthermore, failure can occur at any stage of the trials, and we could encounter problems that cause us to abandon or repeat clinical trials. The commencement and completion of clinical trials may be delayed by several factors, including:

imposition of a clinical hold or failure to obtain regulatory authorization or approval to commence a trial;

unforeseen safety issues;

determination of dosing issues;

lack of effectiveness during clinical trials;

inability to reach agreement on acceptable terms with prospective clinical research organizations and clinical trial sites;

slower-than-expected rates of patient recruitment;

failure to manufacture sufficient quantities of a drug candidate for use in clinical trials;

inability to monitor patients adequately during or after treatment; and

inability or unwillingness of medical investigators to follow our clinical protocols.

Further, we, the FDA or an Institutional Review Board, or IRB, may suspend our clinical trials at any time if it appears that we or our collaborators are failing to conduct a trial in accordance with regulatory requirements, that we are exposing participants to unacceptable health risks, or if the FDA finds deficiencies in our IND submissions or the conduct of these trials. Therefore, we cannot predict with any certainty the schedule for commencement and completion of future clinical trials. If we experience delays in the commencement or completion of our clinical trials, or if we terminate a clinical trial prior to completion, the commercial prospects of our drug candidates could be harmed, and our ability to generate revenues from the drug candidates may be delayed. In addition, any delays in our clinical trials could increase our costs, slow down the approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, financial condition and results

of operations.

Enrollment and retention of patients in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside our control.

We may encounter delays in enrolling, or be unable to enroll, a sufficient number of patients to complete any of our clinical trials, and even once enrolled we may be unable to retain a sufficient number of patients to complete any of our trials. Patient enrollment and retention in clinical trials depends on many factors, including the size of the patient population, the nature of the trial protocol, the existing body of safety and efficacy data with respect to the study drug, the number and nature of competing treatments and on-going clinical trials of competing drugs for the same indication, the proximity of patients to clinical sites and the eligibility criteria for the study. Furthermore, any negative results we may report in clinical trials of any of our drug candidates may make it difficult or impossible to recruit and retain patients in other clinical studies of that same drug candidate. Delays or failures in planned patient enrollment and/or retention may result in increased costs, program delays or both, which could have a harmful effect on our ability to develop our drug candidates, or could render further development impossible. In addition, we expect to rely on clinical research organizations and clinical trial sites to ensure proper and timely conduct of our future clinical trials and, while we intend to enter into agreements governing their services, we will be limited in our ability to compel their actual performance.

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Even if our clinical trials are completed as planned, we cannot be certain that their results will support the safety and effectiveness of our drug candidates for our targeted indications. Success in pre-clinical testing and early clinical trials does not ensure that later clinical trials will be successful, and we cannot be sure that the results of later clinical trials will replicate the results of prior clinical trials and pre-clinical testing. A failure of a clinical trial to meet its predetermined endpoints would likely cause us to abandon a drug candidate and may delay development of other drug candidates. Any delay in, or termination of, our clinical trials will delay the filing of our NDAs with the FDA and, ultimately, our ability to commercialize our drug candidates and generate product revenues.

While we have negotiated a special protocol assessment agreement with the FDA relating to our Phase III clinical study of PB272, this agreement does not guarantee approval of PB272 or any other particular outcome from regulatory review of the clinical trial or the drug candidate.

In February 2013, we announced that we reached agreement with the FDA under a special protocol assessment, or SPA, for our Phase III clinical trial of PB272 in patients with HER2-positive metastatic breast cancer who have failed two or more prior treatments. We commenced the Phase III clinical trial in June 2013. The FDA's SPA process is designed to facilitate the FDA's review and approval of drugs by allowing the FDA to evaluate the proposed design and size of Phase III clinical trials that are intended to form the primary basis for determining a drug product's efficacy. Upon specific request by a clinical trial sponsor, the FDA will evaluate the protocol and respond to a sponsor's questions regarding, among other things, primary efficacy endpoints, trial conduct and data analysis, within 45 days of receipt of the request. The FDA ultimately assesses whether the protocol design and planned analysis of the trial are acceptable to support regulatory approval of the product candidate with respect to the effectiveness of the identified indication. All agreements between the FDA and the sponsor regarding an SPA must be clearly documented in writing, either in the form of an SPA letter or minutes of a meeting between the sponsor and the FDA at which the SPA agreement was reached. However, an SPA agreement does not guarantee approval of a product candidate, and even if the FDA agrees to the design, execution, and analysis proposed in protocols reviewed under the SPA process, the FDA may revoke or alter its agreement in certain circumstances. In particular, an SPA agreement is not binding on the FDA if public health concerns emerge that were unrecognized at the time of the SPA agreement, other new scientific concerns regarding product safety or efficacy arise, the sponsor company fails to comply with the agreed upon trial protocols, or the relevant data, assumptions or information provided by the sponsor in a request for the SPA change or are found to be false or omit relevant facts. In addition, even after an SPA agreement is finalized, the SPA agreement may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if the FDA and the sponsor agree in writing to modify the protocol and such modification is intended to improve the study. The FDA retains significant latitude and discretion in interpreting the terms of the SPA agreement and the data and results from any study that is the subject of the SPA agreement.

We cannot assure you that our Phase III clinical trial will succeed, or that the SPA will ultimately be binding on the FDA or will result in any FDA approval for PB272. The trial is expected to enroll approximately 600 patients. We expect that the FDA will review our compliance with the SPA, evaluate the results of the clinical trials and conduct inspections of some of the approximately 150 sites in North America, Europe and Asia-Pacific where the clinical trials will be conducted. We cannot assure you that each of the clinical trial sites will pass such FDA inspections, and negative inspection results could significantly delay or prevent any potential approval for PB272. If the FDA revokes or alters its agreement under the SPA, or interprets the data collected from the clinical trial differently than we do, the FDA may deem the data insufficient to support regulatory approval, which could materially adversely affect our business, financial condition and results of operations.

Physicians and patients may not accept and use our drugs.

Even if the FDA approves one or more of our drug candidates, physicians and patients may not accept and use them. Acceptance and use of our product will depend upon a number of factors including:

perceptions by members of the health care community, including physicians, about the safety and effectiveness of our drug;

cost-effectiveness of our products relative to competing products;

availability of coverage and reimbursement for our products from government or other healthcare payors;
and

effectiveness of marketing and distribution efforts by us and our licensees and distributors, if any.

Because we expect sales of our current drug candidates, if approved, to generate substantially all of our product revenues for the foreseeable future, the failure of these drugs to find market acceptance would harm our business and could require us to seek additional financing.

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We rely on third parties to conduct our pre-clinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for our drug candidates.

We depend upon independent investigators and collaborators, such as clinical research organizations, universities and medical institutions, to conduct our pre-clinical studies and clinical trials under agreements with us. These collaborators are not our employees and we cannot control the amount or timing of resources that they devote to our programs. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with regulatory requirements and the applicable protocol. These investigators may not assign as great a priority to our programs or pursue them as diligently as we would if we were undertaking such programs ourselves. If outside collaborators fail to devote sufficient time and resources to our drug-development programs, or if their performance is substandard or otherwise fails to satisfy applicable regulatory requirements, the approval of our FDA applications, if any, and our introduction of new drugs, if any, will be delayed. These collaborators may also have relationships with other commercial entities, some of whom may compete with us. If our collaborators assist our competitors to our detriment, our competitive position would be harmed. If any of our relationships with these third-party collaborators terminate, we may not be able to enter into arrangements with alternative third parties on commercially reasonable terms, or at all. Switching or adding additional third parties to our clinical trial programs can involve substantial costs and require extensive management time and focus.

We will rely exclusively on third parties to formulate and manufacture our drug candidates. The commercialization of any of our drug candidates could be stopped, delayed or made less profitable if those third parties fail to provide us with sufficient quantities of product or fail to do so at acceptable quality levels or prices.

We have no experience in drug formulation or manufacturing and do not intend to establish our own manufacturing facilities. We lack the resources and expertise to formulate or manufacture our own drug candidates. While our drug candidates were being developed by Pfizer, both the drug substance and drug product were manufactured by third-party contractors. We are using the same third-party contractors to manufacture, supply, store and distribute drug supplies for our clinical trials. If we are unable to continue our relationships with one or more of these third-party contractors, we could experience delays in our development efforts as we locate and qualify new manufacturers. If any of our current drug candidates, or any drug candidates we may develop or acquire in the future, receive FDA approval, we intend to rely on one or more third-party contractors to manufacture the commercial supply of our drugs. Our anticipated future reliance on a limited number of third-party manufacturers exposes us to the following risks:

We may be unable to identify manufacturers on acceptable terms or at all because the number of potential manufacturers is limited and the FDA must approve any replacement manufacturer. This approval would require new testing and compliance inspections. In addition, a new manufacturer would have to be educated in, or develop substantially equivalent processes for, production of our products after receipt of FDA approval, if any.

Our third-party manufacturers might be unable to formulate and manufacture our drugs in the volume and of the quality required to meet our clinical needs and commercial needs, if any.

Our future contract manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to supply our clinical trials or to successfully produce, store

and distribute our products.

Drug manufacturers are subject to on-going periodic unannounced inspection by the FDA, the Drug Enforcement Administration, similar non-U.S. regulatory agencies and corresponding state agencies to ensure strict compliance with regulations on current good manufacturing practices, or cGMPs, and other government regulations and corresponding foreign standards. We do not have control over third-party manufacturers' compliance with these regulations and standards.

If any third-party manufacturer makes improvements in the manufacturing process for our products, we may not own, or may have to share, the intellectual property rights to the innovation.

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Each of these risks could delay our clinical trials, the approval, if any, of our drug candidates by the FDA or the commercialization of our drug candidates or result in higher costs or deprive us of potential product revenues.

We have no experience selling, marketing or distributing products and no internal capability to do so.

We currently have no sales, marketing or distribution capabilities. We do not anticipate having the resources in the foreseeable future to allocate to the sales and marketing of our proposed products. Our future success will depend, in part, on our ability to enter into and maintain collaborative relationships for such capabilities, the collaborator's strategic interest in the products under development and such collaborator's ability to successfully market and sell any such products. We intend to pursue collaborative arrangements regarding the sale and marketing of our products if and when they are approved; however, we cannot assure you that we will be able to establish or maintain such collaborative arrangements, or if able to do so, that they will have effective sales forces. To the extent that we decide not to, or are unable to, enter into collaborative arrangements with respect to the sales and marketing of our proposed products, significant capital expenditures, management resources and time will be required to establish and develop an in-house marketing and sales force with technical expertise. We also cannot assure you that we will be able to establish or maintain relationships with third-party collaborators or develop in-house sales and distribution capabilities. To the extent that we depend on third parties for marketing and distribution, any revenues we receive will depend upon the efforts of such third parties, and there can be no assurance that such efforts will be successful. In addition, there can also be no assurance that we will be able to market and sell our products in the United States or overseas.

We rely significantly on information technology and any failure, inadequacy, interruption or security lapse of that technology, including any cybersecurity incidents, could harm our ability to operate our business effectively.

Our internal computer systems and those of third parties with which we contract may be vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures despite the implementation of security measures. System failures, accidents or security breaches could cause interruptions in our operations, and could result in a material disruption of our clinical activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. The loss of clinical trial data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and our research and development programs and the development of our product candidates could be delayed.

Health care reform measures may hinder or prevent our drug candidates' commercial success.

The United States and some foreign jurisdictions have enacted or are considering enacting a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to profitably sell our products, if and when they are approved. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, ACA, became law in the United States. ACA substantially changed and will continue to change the way healthcare is financed by both governmental and private insurers and significantly affects the pharmaceutical industry. Among the provisions of ACA, of greatest importance to the pharmaceutical industry are

the following:

an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;

an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;

addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;

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a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;

extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;

expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals, which began in April 2010 and by adding new eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level beginning in 2014, thereby potentially increasing manufacturers' Medicaid rebate liability;

increase in the number of entities eligible for discounts under the Public Health Service pharmaceutical pricing program;

a new requirement to annually report drug samples that manufacturers and distributors provide to physicians;

a licensure framework for follow-on biologic products; and

a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

The ACA also requires adults not covered by employer or government-sponsored insurance plans to maintain health insurance coverage or pay a penalty, a provision commonly referred to as the individual mandate. In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect on April 1, 2013. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, or ATRA, which, among other things, also reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. We cannot predict all of the ways in which future federal or state legislative or administrative changes relating to healthcare reform will affect our business.

Nevertheless, we anticipate that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product, and could seriously harm our business. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Thus, we expect to experience pricing pressures in connection with the sale of neratinib (oral), neratinib (intravenous), PB357 and any other products that we may develop, due to the trend toward managed healthcare, the increasing influence of health

maintenance organizations and additional legislative proposals. There may be additional pressure by payors and healthcare providers to use generic drugs that contain the active ingredients found in neratinib (oral), neratinib (intravenous), PB357 or any other drug candidates that we may develop. If we fail to successfully secure and maintain adequate coverage and reimbursement for our products or are significantly delayed in doing so, we will have difficulty achieving market acceptance of our products and expected revenue and profitability which would have a material adverse effect on our business, results of operations and financial condition.

We may be subject, directly or indirectly, to federal and state healthcare fraud and abuse and false claims laws and regulations. Prosecutions under such laws have increased in recent years and we may become subject to such litigation. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

If we obtain FDA approval for any of our drug candidates and begin commercializing those products in the United States, our operations will be subject directly or indirectly through our customers, to various state and federal fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute and federal False Claims Act and the state law equivalents of such laws. These laws may impact, among other things, our proposed sales, marketing and education programs.

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The federal Anti-Kickback Statute prohibits persons from knowingly and willingly soliciting, offering, receiving or providing remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual, or the furnishing or arranging for a good or service, for which payment may be made under a federal healthcare program such as the Medicare and Medicaid programs. The Anti-Kickback Statute is broad and, despite a series of narrow safe harbors, prohibits many arrangements and practices that are lawful in businesses outside of the healthcare industry. Penalties for violations of the federal Anti-Kickback Statute include criminal penalties and civil sanctions such as fines, imprisonment and possible exclusion from Medicare, Medicaid and other federal healthcare programs. Many states have also adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, including private insurance programs.

The federal False Claims Act prohibits persons from knowingly filing, or causing to be filed, a false claim, or the knowing use of false statements, to obtain payment from the federal government. Suits filed under the False Claims Act, known as *qui tam* actions, can be brought by any individual on behalf of the government, and such individuals, commonly known as whistleblowers, may share in any amounts paid by the entity to the government in fines or settlement. The frequency of filing *qui tam* actions has increased significantly in recent years, causing greater numbers of pharmaceutical, medical device and other healthcare companies to have to defend False Claims Act actions. When it is determined that an entity has violated the False Claims Act, the entity may be required to pay up to three times the actual damages sustained by the government, plus civil penalties for each separate false claim. Various states have also enacted laws modeled after the federal False Claims Act.

We may also be subject to federal criminal healthcare fraud statutes that were created by the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA. The HIPAA health care fraud statute prohibits, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private payors. A violation of this statute is a felony and may result in fines, imprisonment and/or exclusion from government sponsored programs. The HIPAA false statements statute prohibits, among other things, knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement or representation in connection with the delivery of or payment for healthcare benefits, items or services. A violation of this statute is a felony and may result in fines and/or imprisonment.

ACA, among other things, amends the intent requirement of the federal Anti-Kickback Statute and criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. In addition, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

ACA also enacted new provisions that require manufacturers of drugs, devices, biologics, and medical supplies to report annually to the U.S. Department of Health and Human Services information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations. Manufacturers were required to begin collecting data on August 1, 2013 and will be required to submit reports to the government by March 31, 2014, and by the 90th day of each subsequent calendar year. In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians. Certain states mandate implementation of commercial compliance programs, impose restrictions on drug manufacturer marketing practices, and/or the tracking and reporting of gifts, compensation and other remuneration to physicians.

We are unable to predict whether we could be subject to actions under any of these or other fraud and abuse laws, or the impact of such actions. If we are found to be in violation of any of the laws described above and other applicable

state and federal fraud and abuse laws, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from government healthcare reimbursement programs and the curtailment or restructuring of our operations, any of which could have a material adverse effect on our business and results of operations.

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If we cannot compete successfully for market share against other drug companies, we may not achieve sufficient product revenue and our business will suffer.

The market for our drug candidates is characterized by intense competition and rapid technological advances. If any of our drug candidates receives FDA approval, it will compete with a number of existing and future drugs and therapies developed, manufactured and marketed by others. Existing or future competing products may provide greater therapeutic convenience or clinical or other benefits for a specific indication than our products, or may offer comparable performance at a lower cost. In addition, a large number of companies are pursuing the development of pharmaceuticals that target the same diseases and conditions that we are targeting. If our products fail to capture and maintain market share, we may not achieve sufficient product revenue and our business will suffer.

We will compete against fully integrated pharmaceutical companies and smaller companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. Many of these competitors have oncology compounds that have already been approved or are in development. In addition, many of these competitors, either alone or together with their collaborative partners, operate larger research and development programs or have substantially greater financial resources than we do, as well as significantly greater experience in the following:

developing drugs;

undertaking pre-clinical testing and clinical trials;

obtaining FDA and other regulatory approvals of drugs;

formulating and manufacturing drugs; and

launching, marketing and selling drugs.

Our ability to generate product revenue will be diminished if our drugs sell for inadequate prices or patients are unable to obtain coverage or adequate levels of reimbursement.

Our ability to commercialize our drugs, alone or with collaborators, will depend in part on the extent to which reimbursement will be available from the following:

government and health administration authorities;

private health maintenance organizations and health insurers; and

other healthcare payors.

Significant uncertainty exists as to the coverage and reimbursement status of newly approved healthcare products. Healthcare payors, including Medicare, are challenging the prices charged for medical products and services. Government and other healthcare payors increasingly attempt to contain healthcare costs by limiting both coverage and the level of reimbursement for drugs. Even if one of our drug candidates is approved by the FDA, insurance coverage may not be available, or reimbursement levels may be inadequate to cover such drug. If government and other healthcare payors do not provide adequate coverage and reimbursement for any of our products, once approved, market acceptance of such product could be reduced.

We may be exposed to liability claims associated with the use of hazardous materials and chemicals.

Our research and development activities may involve the controlled use of hazardous materials and chemicals. Although we believe that our safety procedures for using, storing, handling and disposing of these materials comply with federal, state and local laws and regulations, we cannot completely eliminate the risk of accidental injury or contamination from these materials. In the event of such an accident, we could be held liable for any resulting damages and any liability could materially adversely affect our business, financial condition and results of operations. In addition, the federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous or radioactive materials and waste products may require us to incur substantial compliance costs that could materially adversely affect our business, financial condition and results of operations.

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The loss of one or more key members of our management team could adversely affect our business.

Our success and future growth depends to a significant degree on the skills and continued services of our management team, in particular Alan H. Auerbach, our President and Chief Executive Officer. If Mr. Auerbach resigns or becomes unable to continue in his present role and is not adequately replaced, our business operations could be materially adversely affected. We do not maintain key man life insurance for Mr. Auerbach.

If we are unable to hire additional qualified personnel, our ability to grow our business may be harmed.

As of December 31, 2013, we had 72 employees, including our President and Chief Executive Officer. Our future success depends on our ability to identify, attract, hire, train, retain and motivate other highly skilled scientific, technical, marketing, managerial and financial personnel. Although we will seek to hire and retain qualified personnel with experience and abilities commensurate with our needs, there is no assurance that we will succeed despite their collective efforts. Competition for personnel is intense, and any failure to attract and retain the necessary technical, marketing, managerial and financial personnel would have a material adverse effect on our business, prospects, financial condition and results of operations.

We may not successfully manage our growth.

Our success will depend upon the expansion of our operations and our ability to successfully manage our growth. Our future growth, if any, may place a significant strain on our management and on our administrative, operational and financial resources. Our ability to manage our growth effectively will require us to implement and improve our operational, financial and management systems and to expand, train, manage and motivate our employees. These demands may require the hiring of additional management personnel and the development of additional expertise by management. Any increase in resources devoted to research and product development without a corresponding increase in our operational, financial and management systems could have a material adverse effect on our business, financial condition and results of operations.

We may be adversely affected by the current economic environment.

Our ability to attract and retain collaborators or customers, invest in and grow our business and meet our financial obligations depends on our operating and financial performance, which, in turn, is subject to numerous factors, including the prevailing economic conditions and financial, business and other factors beyond our control, such as the rate of unemployment, the number of uninsured persons in the United States and inflationary pressures. We cannot anticipate all the ways in which the current economic climate and financial market conditions could adversely impact our business.

We are exposed to risks associated with reduced profitability and the potential financial instability of our collaborators or customers, many of which may be adversely affected by volatile conditions in the financial markets. For example, unemployment and underemployment, and the resultant loss of insurance, may decrease the demand for healthcare services and pharmaceuticals. If fewer patients are seeking medical care because they do not have insurance coverage, our collaboration partners or customers may experience reductions in revenues, profitability and/or cash flow that could lead them to modify, delay or cancel orders for our products once commercialized. If collaboration partners or customers are not successful in generating sufficient revenue or are precluded from securing financing, they may not be able to pay, or may delay payment of, accounts receivable that are owed to us. This, in turn, could adversely affect our financial condition and liquidity. In addition, if economic challenges in the United States result in widespread and prolonged unemployment, either regionally or on a national basis, prior to the effectiveness of certain provisions of the ACA, a substantial number of people may become uninsured or underinsured. To the extent economic challenges

result in fewer individuals pursuing or being able to afford our products once commercialized, our business, results of operations, financial condition and cash flows could be adversely affected.

We may incur substantial liabilities and may be required to limit commercialization of our products in response to product liability lawsuits.

The testing and marketing of medical products entail an inherent risk of product liability. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our products. If we are unable to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims, the commercialization of pharmaceutical products we develop, alone or with collaborators, could be prevented or inhibited.

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Our cash and cash equivalents could be adversely affected if the financial institutions in which we hold our cash and cash equivalents fail.

We regularly maintain cash balances at third-party financial institutions in excess of the Federal Deposit Insurance Corporation, or FDIC, insurance limit. While we monitor daily the cash balances in the operating accounts and adjust the balances as appropriate, these balances could be impacted, and there could be a material adverse effect on our business, if one or more of the financial institutions with which we deposit fails or is subject to other adverse conditions in the financial or credit markets. To date, we have experienced no loss or lack of access to our invested cash or cash equivalents; however, we can provide no assurance that access to our invested cash and cash equivalents will not be impacted by adverse conditions in the financial and credit markets.

Our investments in marketable securities are subject to market, interest and credit risk that may reduce their value.

The value of our investments in marketable securities may be adversely affected by changes in interest rates, downgrades in the creditworthiness of bonds we hold, turmoil in the credit markets and financial services industry and by other factors which may result in other than temporary declines in the value of our investments. Decreases in the market value of our marketable securities could have an adverse impact on our statements of financial position, results of operations and cash flow.

Risks Related to Our Intellectual Property

We depend significantly on intellectual property licensed from Pfizer and the termination of this license would significantly harm our business and future prospects.

We depend significantly on our license agreement with Pfizer. Our license agreement with Pfizer may be terminated by Pfizer if we materially breach the agreement and fail to cure our breach during an applicable cure period. Our failure to use commercially reasonable efforts to develop and commercialize licensed products in certain specified major market countries would constitute a material breach of the license agreement. Pfizer may also terminate the license agreement if we become involved in bankruptcy, receivership, insolvency or similar proceedings. In the event our license agreement with Pfizer is terminated, we will lose all of our rights to develop and commercialize the drug candidates covered by such license, which would significantly harm our business and future prospects.

Our proprietary rights may not adequately protect our intellectual property and potential products, and if we cannot obtain adequate protection of our intellectual property and potential products, we may not be able to successfully market our potential products.

Our commercial success will depend in part on obtaining and maintaining intellectual property protection for our products, formulations, processes, methods and other technologies. We will only be able to protect these technologies and products from unauthorized use by third parties to the extent that valid and enforceable intellectual property rights, including patents, cover them, or other market exclusionary rights apply.

The patent positions of pharmaceutical companies, like ours, can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in such companies' patents has emerged to date in the United States. The general environment for pharmaceutical patents outside the United States also involves significant uncertainty. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced, or that the scope of these patent rights could provide a sufficient degree of future protection that could permit us to gain or keep our competitive advantage with respect to these products and technology. For example, we cannot predict:

the degree and range of protection any patents will afford us against competitors, including whether third parties will find ways to make, use, sell, offer to sell or import competitive products without infringing our patents;

if and when patents will issue;

whether or not others will obtain patents claiming inventions similar to those covered by our patents and patent applications; or

whether we will need to initiate litigation or administrative proceedings in connection with patent rights, which may be costly whether we win or lose.

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The patents we have licensed may be subject to challenge and possibly invalidated or rendered unenforceable by third parties. Changes in either the patent laws or in the interpretations of patent laws in the United States or other countries may diminish the value of our intellectual property.

In addition, others may independently develop similar or alternative products and technologies that may be outside the scope of our intellectual property. Furthermore, others may have invented technology claimed by our patents before we or our licensors did so, and they may have filed patents claiming such technology before we did so, weakening our ability to obtain and maintain patent protection for such technology. Should third parties obtain patent rights to similar products or technology, this may have an adverse effect on our business.

We may also rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. Trade secrets, however, are difficult to protect. While we believe that we will use reasonable efforts to protect our trade secrets, our own or our strategic partners' employees, consultants, contractors or advisors may unintentionally or willfully disclose our information to competitors. We seek to protect this information, in part, through the use of non-disclosure and confidentiality agreements with employees, consultants, advisors and others. These agreements may be breached, and we may not have adequate remedies for a breach. In addition, we cannot ensure that those agreements will provide adequate protection for our trade secrets, know-how or other proprietary information or prevent their unauthorized use or disclosure.

To the extent that consultants or key employees apply technological information independently developed by them or by others to our potential products, disputes may arise as to the proprietary rights in such information, which may not be resolved in our favor. Consultants and key employees who work with our confidential and proprietary technologies are required to assign all intellectual property rights in their discoveries to us. However, these consultants or key employees may terminate their relationship with us, and we cannot preclude them indefinitely from dealing with our competitors. If our trade secrets become known to competitors with greater experience and financial resources, the competitors may copy or use our trade secrets and other proprietary information in the advancement of their products, methods or technologies. If we were to prosecute a claim that a third party had illegally obtained and was using our trade secrets, it could be expensive and time consuming and the outcome could be unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets than courts in the United States. Moreover, if our competitors independently develop equivalent knowledge, we would lack any legal or contractual claim to prevent them from using such information, and our business could be harmed.

Our ability to commercialize our potential products will depend on our ability to sell such products without infringing the patent or proprietary rights of third parties. If we are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in that litigation would have a material adverse effect on our business.

Our ability to commercialize our potential products will depend on our ability to sell such products without infringing the patents or other proprietary rights of third parties. Third-party intellectual property rights in our field are complicated and continuously evolving. The coverage of patents is subject to interpretation by the courts, and this interpretation is not always consistent.

Other companies may have or may acquire intellectual property rights that could be enforced against us. If they do so, we may be required to alter our products, formulations, processes, methods or other technologies, obtain a license, assuming one can be obtained, or cease our product-related activities. If our products or technologies infringe the intellectual property rights of others, they could bring legal action against us or our licensors or collaborators claiming damages and seeking to enjoin any activities that they believe infringe their intellectual property rights. If we are sued for patent infringement, we would need to demonstrate that our products or methods of use either do not infringe the

patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving the invalidity of a patent is particularly difficult in the United States, since it requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. If we are found to infringe a third-party patent, we may need to cease the commercial sale of our products.

Because patent applications can take many years to issue, there may be currently pending applications unknown to us or reissue applications that may later result in issued patents upon which our products or technologies may infringe. There could also be existing patents of which we are unaware that our products or technologies may

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infringe. In addition, if third parties file patent applications or obtain patents claiming products or technologies also claimed by us in pending applications or issued patents, we may have to participate in interference proceedings in the U.S. Patent and Trademark Office, or USPTO, to determine priority of invention. If third parties file oppositions in foreign countries, we may also have to participate in opposition proceedings in foreign tribunals to defend the patentability of our filed foreign patent applications. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Additionally, any uncertainties resulting from the initiation and continuation of any litigation may have a material adverse effect on our ability to raise the funds necessary to continue our operations.

If a third party claims that we infringe its intellectual property rights, it could cause our business to suffer in a number of ways, including:

we may become involved in time-consuming and expensive litigation, even if the claim is without merit, the third party's patent is ultimately invalid or unenforceable, or we are ultimately found to have not infringed;

we may become liable for substantial damages for past infringement if a court decides that our technologies infringe upon a third party's patent;

we may be ordered by a court to stop making, selling or licensing our products or technologies without a license from a patent holder, and such license may not be available on commercially acceptable terms, if at all, or may require us to pay substantial royalties or grant cross-licenses to our patents; and

we may have to redesign our products so that they do not infringe upon others' patent rights, which may not be possible or could require substantial investment and/or time.

If any of these events occur, our business could suffer and the market price of our common stock may decline.

As is common in the biotechnology and pharmaceutical industries, we employ individuals who were previously employed at other companies in these industries, including our competitors or potential competitors. We may become subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers, although no such claims are pending. Litigation may be necessary to defend against these claims. Even if we successfully defend any such claims, we may incur substantial costs in such defense, and our management may be distracted by these claims.

Risks Related to This Offering and Owning our Common Stock

Our stock price may fluctuate significantly and you may have difficulty selling your shares based on current trading volumes of our stock. In addition, numerous other factors could result in substantial volatility in the trading price of our stock.

Our common stock has been listed on the New York Stock Exchange, or NYSE, since October 19, 2012. Prior to October 2012, shares of our common stock had been quoted for trading on the OTC Bulletin Board and OTCQB Market in limited volumes. We cannot predict the extent to which investor interest in our company will be sufficient to maintain an active trading market on the NYSE or any other exchange in the future. We have several stockholders,

including affiliated stockholders, who hold substantial blocks of our stock. As of December 31, 2013, we had 28,991,289 shares of common stock outstanding, and stockholders holding at least 5% of our stock, individually or with affiliated entities, collectively beneficially owned or controlled approximately 53.7% of such shares. Sales of large numbers of shares by any of our large stockholders could adversely affect our trading price, particularly given our relatively small historic trading volumes. If stockholders holding shares of our common stock sell, indicate an intention to sell, or if it is perceived that they will sell, substantial amounts of their common stock in the public market, the trading price of our common stock could decline. Moreover, if there is no active trading market or if the volume of trading is limited, holders of our common stock may have difficulty selling their shares.

The price of our common stock could be subject to volatility related or unrelated to our operations.

The trading price of our common stock may be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. These factors include:

actual or anticipated quarterly variation in our results of operations or the results of our competitors;

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announcements of medical innovations or new products by our competitors;

announcements regarding results of any clinical trials relating to our drug candidates;

issuance of new or changed securities analysts' reports or recommendations for our stock;

developments or disputes concerning our intellectual property or other proprietary rights;

commencement of, or involvement in, litigation;

market conditions in the biopharmaceutical industry;

timing and announcement of regulatory approvals;

any future sales of our common stock or other securities in connection with raising additional capital or otherwise;

any major change to the composition of our board of directors or management; and

general economic conditions and slow or negative growth of our markets.

The stock market in general, and market prices for the securities of technology-based companies like ours in particular, have from time to time experienced volatility that often has been unrelated to the operating performance of the underlying companies. These broad market and industry fluctuations may adversely affect the market price of our common stock, regardless of our operating performance. In several recent situations where the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a lawsuit against us, the defense and disposition of the lawsuit could be costly and divert the time and attention of our management and harm our operating results.

Investors in this offering will suffer immediate and substantial dilution of their investment.

If you purchase common stock in this offering, you will pay more for your shares than our net tangible book value per share. Based upon an assumed public offering price of \$ _____ per share, the last reported sale price of our common stock on _____, 2014, you will incur immediate and substantial dilution of \$ _____ per share, representing the difference between our public offering price and our net tangible book value per share as of September 30, 2013. Furthermore, if the underwriters exercise their option to purchase additional shares of our common stock, you could experience further dilution. You will experience additional dilution upon exercise of any warrant, upon exercise of options to purchase common stock under our incentive award plan, or if we otherwise issue additional shares of our common stock. For a further description of the dilution that you will experience immediately after this offering, see Dilution.

Our management will have broad discretion over the use of the proceeds we receive in this offering and might not apply the proceeds in ways that increase the value of your investment.

Our management will have broad discretion to use the net proceeds from this offering, and you will be relying on the judgment of our management regarding the application of these proceeds. Our management might not apply the net proceeds of this offering in ways that increase the value of your investment.

Issuance of stock to fund our operations may dilute your investment and reduce your equity interest.

We may need to raise additional capital in the future to fund the development of our drug candidates or for other purposes. Any equity financing may have a significant dilutive effect to stockholders and a material decrease in our existing stockholders' equity interest in us. Equity financing, if obtained, could result in substantial dilution to our existing stockholders. At its sole discretion, our board of directors may issue additional securities without seeking stockholder approval, and we do not know when we will need additional capital or, if we do, whether it will be available to us.

Upon the exercise of our outstanding warrant, holders of our common stock may experience immediate dilution and the market price of our common stock may be adversely affected.

Following an October 2011 private placement, Alan H. Auerbach, the Company's founder, President and Chief Executive Officer, held approximately 21% of our outstanding shares of common stock. Pursuant to the terms of the Securities Purchase Agreement for the private placement, we issued an anti-dilutive warrant to Mr. Auerbach. The warrant has a 10-year term expiring in October 2021 for 2,116,250 shares with an exercise price of \$16.00 per share.

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If any portion of the outstanding warrant is exercised for shares of our common stock, our stockholders may experience immediate dilution and the market price of our common stock may be adversely affected.

We will incur increased costs and demands upon management as a result of complying with the laws and regulations affecting public companies, which could harm our operating results.

As a public company, we incur significant legal, accounting and other expenses, including costs associated with public company reporting requirements. We also incur costs associated with current corporate governance requirements, including requirements under Section 404 and other provisions of the Sarbanes-Oxley Act of 2002, as amended, or the Sarbanes-Oxley Act, as well as rules implemented by the Securities and Exchange Commission, or the SEC, or the NYSE or any stock exchange or inter-dealer quotations system on which our common stock may be listed in the future. The expenses incurred by public companies for reporting and corporate governance purposes have increased dramatically in recent years. We expect these rules and regulations to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. We are unable to currently estimate these costs with any degree of certainty. We also expect that these new rules and regulations may make it difficult and expensive for us to obtain director and officer liability insurance, and if we are able to obtain such insurance, we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage available to privately-held companies. As a result, it may be more difficult for us to attract and retain qualified individuals to serve on our board of directors or as our executive officers.

If we fail to maintain proper and effective internal controls, our ability to produce accurate and timely financial statements could be impaired, which could harm our operating results, our ability to operate our business and investors' views of us.

We are subject to the rules and regulations of the SEC, including those rules and regulations mandated by the Sarbanes-Oxley Act. Section 404 of the Sarbanes-Oxley Act requires public companies to include in their annual report a statement of management's responsibilities for establishing and maintaining adequate internal control over financial reporting, together with an assessment of the effectiveness of those internal controls. Section 404 also requires the independent auditors of certain public companies to attest to, and report on, this management assessment. We will be required to comply with these requirements in our upcoming annual report on Form 10-K for the year ended December 31, 2013. Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that will need to be evaluated frequently. Our failure to maintain the effectiveness of our internal controls in accordance with the requirements of the Sarbanes-Oxley Act could have a material adverse effect on our business. We could lose investor confidence in the accuracy and completeness of our financial reports, which could have an adverse effect on the price of our common stock. In addition, if our efforts to comply with new or changed laws, regulations, and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to practice, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

The resale of shares covered by a registration statement could adversely affect the market price of our common stock in the public market, should one develop, which result would in turn negatively affect our ability to raise additional equity capital.

The sale, or availability for sale, of our common stock in the public market may adversely affect the prevailing market price of our common stock and may impair our ability to raise additional capital by selling equity or equity-linked securities. Pursuant to the terms of a registration rights agreement, as amended, between us and certain of our stockholders, we maintain an effective registration statement registering the resale of shares of our common stock by certain of our stockholders. As of April 2013, the most recent effective date of the registration statement,

approximately 10,942,158 shares of our common stock remained available for resale under the registration statement. The resale of a substantial number of shares of our common stock in the public market could adversely affect the market price for our common stock and make it more difficult for investors in our common stock to sell shares of our common stock at times and prices that such investors feel are appropriate. Furthermore, we expect that, because there are a large number of shares registered pursuant to the resale registration statement, the selling stockholders identified in such registration statement will continue to offer shares covered by such

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registration statement for a significant period of time, the precise duration of which cannot be predicted. Accordingly, the adverse market and price pressures resulting from offerings pursuant to the registration statement may continue for an extended period of time and continued negative pressure on the market price of our common stock could have a material adverse effect on our ability to raise additional equity capital.

If securities or industry analysts do not publish, or cease publishing, research or reports about us, our business or our market, or if they change their recommendations regarding our stock adversely, our stock price and trading volume could decline.

The trading market for our common stock is and will be influenced by whether industry or securities analysts publish research and reports about us, our business, our market or our competitors and, if any analysts do publish such reports, what they publish in those reports. We may not obtain analyst coverage in the future. Any analysts who do cover us may make adverse recommendations regarding our stock, adversely change their recommendations from time to time, and/or provide more favorable relative recommendations about our competitors. If any analyst who may cover us in the future were to cease coverage of our company or fail to regularly publish reports on us, or if analysts fail to cover us or publish reports about us at all, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

We do not foresee paying cash dividends in the foreseeable future.

We currently intend to retain any future earnings for funding growth. We do not anticipate paying any dividends in the foreseeable future. As a result, you should not rely on an investment in our securities if you require dividend income. Capital appreciation, if any, of our shares may be your sole source of gain for the foreseeable future. Moreover, you may not be able to re-sell your shares in us at or above the price you paid for them.

Our ability to use our net operating losses and research and development credit carryforwards to offset future taxable income may be subject to certain limitations.

In general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an ownership change, generally defined as a greater than 50% change (by value) in its equity ownership over a three year period, is subject to limitations on its ability to utilize its pre-change net operating losses, or NOLs, and its research and development credit carryforwards to offset future taxable income. Our existing NOLs and research and development credit carryforwards may be subject to limitations arising from previous ownership changes, and if we undergo an ownership change, our ability to utilize NOLs and research and development credit carryforwards could be further limited by Sections 382 and 383 of the Code. Future changes in our stock ownership, some of which might be beyond our control, could result in an ownership change under Sections 382 and 383 of the Code. Furthermore, our ability to utilize NOLs and research and development credit carryforwards of any companies we may acquire in the future may be subject to limitations, in accordance with Sections 382 and 383 of the Code. For these reasons, in the event we experience a change of control, we may not be able to utilize a material portion of the NOLs and research and development credit carryforwards, even if we attain profitability.

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CAUTIONARY STATEMENTS REGARDING FORWARD-LOOKING STATEMENTS

This prospectus includes and incorporates forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, which we refer to as the Securities Act, and Section 21E of the Securities Exchange Act of 1934, which we refer to as the Exchange Act. These statements are often, but not always, made through the use of words or phrases such as anticipate, estimate, plan, project, continuing, ongoing, expect, intend and similar words or phrases. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. Accordingly, these statements involve estimates, assumptions, risks and uncertainties, including the risks discussed in the section entitled Risk Factors, that could cause actual results to differ materially from those expressed in them. You should not place undue reliance on these forward-looking statements. Although forward-looking statements reflect management's good faith beliefs, reliance should not be placed on forward-looking statements because they involve known and unknown risks, uncertainties and other factors, which may cause the actual results, performance or achievements to differ materially from anticipated future results, performance or achievements expressed or implied by such forward-looking statements. These forward-looking statements include, but are not limited to, statements about:

the development of our drug candidates, including when we expect to undertake, initiate and complete clinical trials of our product candidates;

the regulatory approval of our drug candidates;

our use of clinical research organizations and other contractors;

our ability to find collaborative partners for research, development and commercialization of potential products;

our ability to market any of our products;

our history of operating losses;

our expectations regarding our costs and expenses;

our anticipated capital requirements and estimates regarding our needs for additional financing;

our ability to compete against other companies and research institutions;

our ability to secure adequate protection for our intellectual property;

our ability to attract and retain key personnel; and

our ability to obtain adequate financing.

Discussions containing these forward-looking statements may be found throughout this prospectus and the information incorporated by reference in this prospectus. Forward-looking statements speak only as of the date the statements are made. We undertake no obligation to update the forward-looking statements or to reflect events or circumstances after the date of this document. The risks discussed in this prospectus should be considered in evaluating our prospects and future financial performance.

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USE OF PROCEEDS

At the assumed public offering price of \$ per share, the last reported sale price of our common stock on , 2014, we estimate that the net proceeds from this offering will be approximately \$ million (or \$ million if the underwriters exercise their option to purchase additional shares in full), after deducting the underwriters discounts and commissions and estimated offering expenses payable by us.

Each \$1.00 increase (decrease) in the assumed public offering price of \$ would increase (decrease) the net proceeds to us from this offering by approximately \$, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, assuming that the number of shares offered by us, as set forth above, remains the same. Each increase (decrease) of 100,000 shares in the number of shares offered by us at the assumed public offering price would increase (decrease) the net proceeds to us in this offering by approximately \$ million. We do not expect that a change in the public offering price or the number of shares by these amounts would have a material effect on our uses of the proceeds from this offering, although it may impact the amount of time prior to which we will need to seek additional capital.

We intend to use the net proceeds to us from this offering for the overall development of our drug candidates, including, but not limited to, research and development and clinical trial expenditures, and for general corporate and working capital purposes. Pending the application of the net proceeds as described above, we intend to invest the net proceeds of the offering in short-term, investment-grade, interest-bearing securities.

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 to us from this offering and investors will be relying on the judgment of our management regarding the application of the proceeds from this offering. We reserve the right to change the use of these proceeds as a result of certain contingencies such as competitive developments, the results of our commercialization efforts, acquisition and investment opportunities and other factors.

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From April 20, 2012, through October 18, 2012, shares of our common stock were quoted on the OTC Bulletin Board, or OTCBB*, under the symbol PBYI. On October 19, 2012, shares of our common stock commenced trading on the NYSE under the symbol PBYI and ceased being quoted on the OTCBB. The high and low bid quotations of our common stock on the OTCBB and the high and low sales prices of our common stock on the NYSE are set forth below:

| Fiscal Year 2012 | High | Low |
|--|-------------|------------|
| First Quarter | \$ | \$ |
| Second Quarter | 14.03 | 10.00 |
| Third Quarter | 15.00 | 11.00 |
| Fourth Quarter | 23.25 | 15.00 |
| OTCBB: October 1 18 | 17.25 | 15.00 |
| NYSE: October 19 December 31 | 23.25 | 16.08 |
| Fiscal Year 2013 | | |
| First Quarter | 34.98 | 18.47 |
| Second Quarter | 45.69 | 27.40 |
| Third Quarter | 62.66 | 44.39 |
| Fourth Quarter | 112.46 | 33.70 |
| Fiscal Year 2014 | | |
| First Quarter (through January 28, 2014) | 143.65 | 99.90 |

* The OTCBB is a quotation medium for subscribing members, not an issuer listing service. OTCBB securities are traded by a community of market makers that enter quotes and trade reports through a closed computer network. The last reported sale price for our common stock on January 28, 2014 was \$125.18 per share. On December 31, 2013, we had 44 holders of record of our common stock. We believe approximately 7,300 additional owners held our common stock in street name as of that date.

DIVIDEND POLICY

We never have declared or paid any cash dividends on our capital stock. Currently, we anticipate that we will retain all available funds for use in the operation and expansion of our business and do not anticipate paying any cash dividends after the offering and for the foreseeable future. Any future determination relating to dividend policy will be made at the discretion of our board of directors and will depend on our future earnings, capital requirements, financial condition, prospects, applicable Delaware law, which provides that dividends are only payable out of surplus or current net profits, and other factors that our board of directors deems relevant.

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If you invest in our common stock in this offering, your ownership interest will be immediately diluted to the extent of the difference between the public offering price per share of our common stock and the as adjusted net tangible book value per share of our common stock upon closing of this offering. Net tangible book value per share of our common stock is determined at any date by subtracting our total liabilities from the amount of our total tangible assets (total assets less intangible assets) and dividing the difference by the number of shares of our common stock deemed to be outstanding at that date.

Our net tangible book value as of September 30, 2013 was approximately \$94.8 million, or \$3.30 per share, based on 28,689,304 shares of common stock outstanding as of September 30, 2013. After giving effect to our sale of shares of common stock in this offering at an assumed public offering price of \$ _____ per share, the last reported sale price of our common stock on _____, 2014, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2013 would have been \$ _____, or \$ _____ per share. This amount represents an immediate increase in net tangible book value of \$ _____ per share of our common stock to existing stockholders and an immediate dilution in net tangible book value of \$ _____ per share of our common stock to new investors purchasing shares of common stock in this offering.

The following tables illustrate this dilution on a per share basis:

| | | |
|---|----|------|
| Assumed public offering price per share | \$ | |
| Net tangible book value per share as of September 30, 2013 before giving effect to the offering of shares by us | \$ | 3.30 |
| Increase in net tangible book value per share attributable to new investors | | |
| As adjusted net tangible book value per share after this offering | \$ | |
| Dilution per share to new investors in this offering | \$ | |

Each \$1.00 increase (decrease) in the assumed public offering price would increase (decrease) our as adjusted net tangible book value by \$ _____, our as adjusted net tangible book value per share after this offering by \$ _____ per share and the dilution per share to new investors in this offering by \$ _____ per share, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same. Each increase of 100,000 shares in the number of shares offered by us at the assumed public offering price would increase our as adjusted net tangible book value by \$ _____, our as adjusted net tangible book value per share after this offering by \$ _____ per share and the dilution per share to new investors in this offering by \$ _____ per share. Similarly, each decrease of 100,000 shares in the number of shares offered by us at the assumed public offering price would decrease our as adjusted net tangible book value by \$ _____, our as adjusted net tangible book value per share after this offering by \$ _____ per share and the dilution per share to new investors in this offering by \$ _____ per share.

If the underwriters exercise their option to purchase additional shares of our common stock in full, the as adjusted net tangible book value per share after giving effect to this offering would be \$ _____ per share, which amount represents an immediate increase in as adjusted net tangible book value of \$ _____ per share of our common stock to existing stockholders and an immediate dilution per share to new investors in this offering of \$ _____ per share.

The discussion and table above exclude, as of September 30, 2013:

2,373,309 shares of common stock issuable upon the exercise of options outstanding as of September 30, 2013 at a weighted average exercise price of \$14.76 per share;

1,143,465 shares of common stock reserved for future issuance under our incentive award plan; and

2,116,250 shares of our common stock issuable upon the exercise of a warrant held by Alan Auerbach, our President and Chief Executive Officer, at \$16.00 per share.

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In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital by issuing equity securities or convertible debt, your ownership will be further diluted.

Table of Contents**CAPITALIZATION**

The following table sets forth our cash and cash equivalents and our capitalization as of September 30, 2013 on:

an actual basis; and

an as adjusted basis giving additional effect to the sale of _____ shares of our common stock offered in this offering at an assumed public offering price of \$ _____ per share, the last reported sale price of our common stock set forth on the cover page of this prospectus, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

The information in this table is illustrative only and our capitalization following the closing of this offering will be adjusted based on the actual public offering price. You should read this table in conjunction with the information contained in Use of Proceeds, Summary Financial Data and Management's Discussion and Analysis of Financial Condition and Results of Operations, as well as our financial statements and the notes thereto included elsewhere or incorporated by reference in this prospectus.

| (in thousands except share data) | As of September 30, 2013 | |
|--|--------------------------|--------------------|
| | Actual | As Adjusted (1) |
| Cash and cash equivalents | \$ 51,261 | \$ |
| Marketable securities | 44,377 | |
| Common stock: \$0.0001 par value, 100,000,000 shares authorized, 28,689,304 shares issued and outstanding (actual); \$0.0001 par value, 100,000,000 shares authorized, shares issued and outstanding (as adjusted) | 3 | |
| Additional paid-in capital | 218,070 | |
| Accumulated deficit | (123,305) | |
| Total stockholders' equity | 94,760 | |
| Total capitalization | 115,109 | |

- (1) Each \$1.00 increase (decrease) in the assumed public offering price would increase (decrease) cash and cash equivalents, additional paid-in capital, total stockholders' equity and total capitalization by approximately \$ _____ million, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same. Each increase (decrease) of 100,000 shares in the number of shares offered by us at the assumed public offering price would increase cash and cash equivalents, additional paid-in capital, total stockholders' equity and total capitalization by approximately \$ _____ million. The as adjusted information discussed above is illustrative only and will be adjusted based on the actual public offering price and other terms of this offering determined at pricing.

The information in the above table excludes, as of September 30, 2013:

2,373,309 shares of common stock issuable upon the exercise of options outstanding as of September 30, 2013 at a weighted average exercise price of \$14.76 per share;

1,143,465 shares of common stock reserved for future issuance under our incentive award plan; and

2,116,250 shares of our common stock issuable upon the exercise of a warrant held by Alan Auerbach, our President and Chief Executive Officer, at \$16.00 per share.

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DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock is only a summary, and is qualified in its entirety by reference to the actual terms and provisions of the capital stock contained in our certificate of incorporation, our bylaws, and other agreements to which we and our stockholders are parties.

General

We currently have authorized capital stock of 100,000,000 shares, which are designated as common stock, par value \$0.0001 per share. As of December 31, 2013, we had 28,991,289 shares of common stock outstanding held of record by 44 stockholders. Since many stockholders hold shares in street name, we believe that the number of beneficial owners of shares of our common stock was significantly larger than the number of record holders. In addition, as of December 31, 2013, there were outstanding options to purchase 2,604,224 shares of common stock.

The holders of our common stock are entitled to one vote per share on matters on which our stockholders vote. There are no cumulative voting rights. Holders of our common stock are entitled to receive dividends, if declared by our board of directors, out of funds that we may legally use to pay dividends. If we liquidate or dissolve, holders of our common stock are entitled to share ratably in our assets once our debts are paid. Our amended and restated certificate of incorporation does not provide our common stock with any redemption, conversion or preemptive rights.

Dividend Policy

In the past, we have not distributed earnings to stockholders. Any future decisions regarding dividends will be made by our board of directors. We currently intend to retain and use any future earnings for the development and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. Our board of directors has complete discretion on whether to pay dividends. Even if our board of directors decides to pay dividends, the form, frequency and amount will depend upon our future operations and earnings, capital requirements and surplus, general financial condition, contractual restrictions and other factors that the board may deem relevant.

Registration Rights

Pursuant to the terms of a registration rights agreement, as amended, between us and certain of our stockholders, we maintain an effective registration statement registering the resale of shares of our common stock by certain of our stockholders. As of April 2013, the most recent effective date of the registration statement, approximately 10,942,158 shares of our common stock remained available for resale under the registration statement. If we do not, subject to certain exceptions, maintain the effectiveness of this registration statement until the second anniversary of the date this registration statement is initially declared effective, or until February 14, 2014, or if we suspend the use of this registration statement in excess of permitted periods, then we will also be required to pay liquidated damages, on a 30-day basis, to each investor equal to 1.0% of the aggregate purchase price paid by the investor for the registrable shares of our common stock then held by the investor; provided, however, that the aggregate amount of liquidated damages payable by us to each investor as a result of our suspension or failure to maintain the effectiveness of the registration statement shall not exceed 10.0% of the aggregate purchase price paid by the investor in the private placement. The registration rights agreement, as amended, also gives investors certain co-sale rights with respect to a firm commitment underwritten offering of the shares of our common stock held by Alan H. Auerbach, our President and Chief Executive Officer.

Warrant

In October 2011, Alan H. Auerbach, our Chairman, Chief Executive Officer and President was issued a warrant that entitled him to maintain ownership of at least 20% of our common stock following our public offering that closed in October 2012. The warrant entitles Mr. Auerbach to acquire 2,116,250 shares of our common stock at \$16 per share. The warrant is exercisable until October 2021.

Indemnification of Directors and Officers

Section 145 of the Delaware General Corporation Law authorizes a corporation to grant, and authorizes a court to award, indemnity to officers, directors and other corporate agents. As permitted by Section 102(b)(7) of the Delaware General Corporation Law, our certificate of incorporation includes a provision that eliminates the personal liability of our directors for breach of their fiduciary duty as directors, except that a director shall be liable to the extent provided by applicable law (i) for breach of the director's duty of loyalty to us or our stockholders, (ii) for

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acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) pursuant to Section 174 of the Delaware General Corporation Law or (iv) for any transaction from which the director derived an improper personal benefit. These indemnification provisions may be sufficiently broad to permit indemnification of our officers and directors for liabilities (including reimbursement of expenses incurred) arising under the Securities Act.

To the extent that indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling our Company pursuant to the foregoing provisions, we have 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. If a claim for indemnification against such liabilities (other than the payment by us of expenses incurred or paid by a director, officer or controlling person of our company in the successful defense of any action, suit or proceeding) is asserted by any of our directors, officers or controlling persons in connection with the securities being registered, we will, unless in the opinion of our counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by us is against public policy as expressed in the Securities Act and will be governed by the final adjudication of that issue.

Delaware Anti-Takeover Statute

We are subject to Section 203 of the Delaware General Corporation Law. This statute regulating corporate takeovers prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for three years following the date that the stockholder became an interested stockholder, unless:

prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;

upon completion of the transaction that resulted in the interested 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 number of shares outstanding (a) shares owned by persons who are directors and also officers, and (b) shares owned by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

on or subsequent to the date of the transaction, 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.

Generally, a business combination includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is any person who, together with such person's affiliates and associates (i) owns 15% or more of a corporation's voting securities or (ii) is an affiliate or associate of a corporation and was the owner of 15% or more of the corporation's voting securities at any time within the three-year period immediately preceding a business combination of the corporation governed by Section 203. We expect the existence of this provision to have an anti-takeover effect with respect to transactions our board of directors does not approve in advance. We also anticipate that Section 203 may discourage takeover attempts that might result in a premium over the market price, once a market exists, for the shares of common stock held by our stockholders.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Wells Fargo Bank, N.A. The transfer agent's address is Wells Fargo Shareowner Services, 1110 Centre Pointe Curve, Suite 101, Mendota Heights, Minnesota 55120, and its telephone number is (800) 468-9716.

Book Entry; Uncertificated Shares

The common stock sold in this offering will be issued in book-entry form through the direct registration system. Under this system, unless a common stockholder requests a physical stock certificate, ownership of our common stock is reflected in account statements periodically distributed to our common stockholders by our transfer agent, who will hold the book-entry shares on behalf of our common stockholders. However, any holder of our common stock who wishes to receive a physical stock certificate evidencing his, her or its shares of our common stock may at any time obtain a stock certificate at no charge by contacting our transfer agent.

New York Stock Exchange Listing

Our common stock is listed on the New York Stock Exchange under the symbol **PBYI**.

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MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS

The following discussion is a summary of the material U.S. federal income tax consequences to Non-U.S. Holders (as defined below) of the purchase, ownership and disposition of our common stock issued pursuant to this offering, but does not purport to be a complete analysis of all potential tax effects. The effects of other U.S. federal tax laws, such as estate and gift tax laws, and any applicable state, local or non-U.S. tax laws are not discussed. This discussion is based on the U.S. Internal Revenue Code of 1986, as amended (the Code), Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the U.S. Internal Revenue Service (the IRS), in each case in effect as of the date hereof. These authorities may change or be subject to differing interpretations. Any such change or differing interpretation may be applied retroactively in a manner that could adversely affect a Non-U.S. Holder of our common stock. We have not sought and will not seek any rulings from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a contrary position to that discussed below regarding the tax consequences of the purchase, ownership and disposition of our common stock.

This discussion is limited to Non-U.S. Holders that hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all U.S. federal income tax consequences relevant to a Non-U.S. Holder's particular circumstances, including the impact of the Medicare contribution tax on net investment income. In addition, it does not address consequences relevant to Non-U.S. Holders subject to special rules, including, without limitation:

U.S. expatriates and former citizens or long-term residents of the United States;

persons subject to the alternative minimum tax;

persons holding our common stock as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;

banks, insurance companies, and other financial institutions;

real estate investment trusts or regulated investment companies;

brokers, dealers or traders in securities;

controlled foreign corporations, passive foreign investment companies, and corporations that accumulate earnings to avoid U.S. federal income tax;

partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and investors therein);

tax-exempt organizations or governmental organizations;

persons deemed to sell our common stock under the constructive sale provisions of the Code;

persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation; and

tax-qualified retirement plans.

If an entity treated as a partnership for U.S. federal income tax purposes holds our common stock, the tax treatment of a partner in the partnership will depend on the status of the partner, the activities of the partnership and certain determinations made at the partner level. Accordingly, partnerships holding our common stock and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

THIS DISCUSSION IS FOR INFORMATIONAL PURPOSES ONLY AND IS NOT TAX ADVICE. INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

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Definition of a Non-U.S. Holder

For purposes of this discussion, a **Non-U.S. Holder** is any beneficial owner of our common stock that is neither a U.S. person nor an entity treated as a partnership for U.S. federal income tax purposes. A U.S. person is any person that, for U.S. federal income tax purposes, is or is treated as any of the following:

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

a corporation created or organized under the laws of the United States, any state thereof, or the District of Columbia;

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

a trust that (1) is subject to the primary supervision of a U.S. court and the control of one or more United States persons (within the meaning of Section 7701(a)(30) of the Code), or (2) has a valid election in effect to be treated as a United States person for U.S. federal income tax purposes.

Distributions

As described in the section entitled **Dividend Policy**, we do not anticipate declaring or paying dividends to holders of our common stock in the foreseeable future. However, if we do make distributions of cash or property on our common stock, such distributions 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. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and first be applied against and reduce a Non-U.S. Holder's adjusted tax basis in its common stock, but not below zero. Any excess will be treated as capital gain and will be treated as described below under **Sale or Other Taxable Disposition**.

Subject to the discussion below on effectively connected income, dividends paid to a Non-U.S. Holder of our common stock will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends (or such lower rate specified by an applicable income tax treaty, provided the Non-U.S. Holder furnishes a valid IRS Form W-8BEN (or other applicable documentation) certifying qualification for the lower treaty rate). A Non-U.S. Holder that does not timely furnish the required documentation, but that qualifies for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. Non-U.S. Holders should consult their tax advisors regarding their entitlement to benefits under any applicable income tax treaty.

If dividends paid to a Non-U.S. Holder are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such dividends are attributable), the Non-U.S. Holder will be exempt from the U.S. federal withholding tax described above. To claim the exemption, the Non-U.S. Holder must furnish to the applicable withholding agent a valid IRS Form W-8ECI, certifying that the dividends are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States.

Any such effectively connected dividends will be subject to U.S. federal income tax on a net income basis at the regular graduated rates. A Non-U.S. Holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected dividends, as adjusted for certain items. Non-U.S. Holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

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Sale or Other Taxable Disposition

A Non-U.S. Holder will not be subject to U.S. federal income tax on any gain realized upon the sale 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 within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such gain is attributable);

the Non-U.S. Holder is a nonresident alien individual present in the United States for 183 days or more during the taxable year of the disposition and certain other requirements are met; or

our common stock constitutes a U.S. real property interest ("USRPI") by reason of our status as a U.S. real property holding corporation ("USRPHC") for U.S. federal income tax purposes.

Gain described in the first bullet point above generally will be subject to U.S. federal income tax on a net income basis at the regular graduated rates. A Non-U.S. Holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected gain, as adjusted for certain items.

Gain described in the second bullet point above will be subject to U.S. federal income tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty), which may be offset by U.S. source capital losses of the Non-U.S. Holder (even though the individual is not considered a resident of the United States), provided the Non-U.S. Holder has timely filed U.S. federal income tax returns with respect to such losses.

With respect to the third bullet point above, we believe we currently are not, and do not anticipate becoming, a USRPHC. Because the determination of whether we are a USRPHC depends, however, on the fair market value of our USRPIs relative to the fair market value of our non-U.S. real property interests and our other business assets, there can be no assurance we currently are not a USRPHC or will not become one in the future. Even if we are or were to become a USRPHC, gain arising from the sale or other taxable disposition by a Non-U.S. Holder of our common stock will not be subject to U.S. federal income tax if our common stock is regularly traded, as defined by applicable Treasury Regulations, on an established securities market, and such Non-U.S. Holder owned, actually or constructively, 5% or less of our common stock throughout the shorter of the five-year period ending on the date of the sale or other taxable disposition or the Non-U.S. Holder's holding period.

Non-U.S. Holders should consult their tax advisors regarding potentially applicable income tax treaties that may provide for different rules.

Information Reporting and Backup Withholding

Payments of dividends on our common stock will not be subject to backup withholding, provided the applicable withholding agent does not have actual knowledge or reason to know the holder is a United States person and the holder either certifies its non-U.S. status, such as by furnishing a valid IRS Form W-8BEN or W-8ECI, or otherwise establishes an exemption. However, information returns are required to be filed with the IRS in connection with any dividends on our common stock paid to the Non-U.S. Holder, regardless of whether any tax was actually withheld. In

addition, proceeds of the sale or other taxable disposition of our common stock within the United States or conducted through certain U.S.-related brokers generally will not be subject to backup withholding or information reporting, if the applicable withholding agent receives the certification described above and does not have actual knowledge or reason to know that such holder is a United States person, or the holder otherwise establishes an exemption. Proceeds of a disposition of our common stock conducted through a non-U.S. office of a non-U.S. broker generally will not be subject to backup withholding or information reporting.

Copies of information returns that are filed with the IRS may also be made available under the provisions of an applicable treaty or agreement to the tax authorities of the country in which the Non-U.S. Holder resides or is established.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a Non-U.S. Holder's U.S. federal income tax liability, provided the required information is timely furnished to the IRS.

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Additional Withholding Tax on Payments Made to Foreign Accounts

Withholding taxes may be imposed under Sections 1471 to 1474 of the Code (such Sections commonly referred to as the Foreign Account Tax Compliance Act, or FATCA) on certain types of payments made to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a foreign financial institution or a non-financial foreign entity (each as defined in the Code), unless (1) the foreign financial institution undertakes certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any substantial United States owners (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (1) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain specified United States persons or United States-owned foreign entities (each as defined in the Code), annually report certain information about such accounts, and withhold 30% on certain payments to non-compliant foreign financial institutions and certain other account holders. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules.

Under the applicable Treasury Regulations and IRS guidance, withholding under FATCA generally will apply to payments of dividends on our common stock made on or after July 1, 2014 and to payments of gross proceeds from the sale or other disposition of such stock on or after January 1, 2017.

Prospective investors should consult their tax advisors regarding the potential application of withholding under FATCA to their investment in our common stock.

Table of Contents**UNDERWRITING**

Merrill Lynch, Pierce, Fenner & Smith Incorporated, Citigroup Global Markets Inc. and Leerink Partners LLC are acting as representatives of each of the underwriters named below. Subject to the terms and conditions set forth in an underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of shares of common stock set forth opposite its name below.

| Underwriter | Number of Shares |
|--|-------------------------|
| Merrill Lynch, Pierce, Fenner & Smith Incorporated | |
| Citigroup Global Markets Inc. | |
| Leerink Partners LLC | |
| Total | |

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the underwriting agreement may be terminated.

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

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officer's certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representatives have advised us that the underwriters propose initially to offer the shares to the public at the public offering price set forth on the cover page of this prospectus and to dealers at that price less a concession not in excess of \$ _____ per share. After the initial offering, the public offering price, concession or any other term of the offering may be changed.

The following table shows the public offering price, underwriting discount and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their option to purchase additional shares.

| | Per Share | Without Option | With Option |
|----------------------------------|------------------|-----------------------|--------------------|
| Public offering price | \$ | \$ | \$ |
| Underwriting discount | \$ | \$ | \$ |
| Proceeds, before expenses, to us | \$ | \$ | \$ |

The expenses of the offering, not including the underwriting discount, are estimated at \$ _____ and are payable by us.

Option to Purchase Additional Shares

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus, to purchase up to _____ additional shares at the public offering price, less the underwriting discount. If the underwriters exercise this option, each will be obligated, subject to conditions contained in the underwriting agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table.

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No Sales of Similar Securities

We, our executive officers, directors and certain of our stockholders have agreed not to sell or transfer any common stock or securities convertible into, exchangeable for, exercisable for, or repayable with common stock, for 90 days after the date of this prospectus without first obtaining the written consent of the representatives. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly:

offer, pledge, sell or contract to sell any common stock,

sell any option or contract to purchase any common stock,

purchase any option or contract to sell any common stock,

grant any option, right or warrant for the sale of any common stock,

lend or otherwise dispose of or transfer any common stock,

request or demand that we file a registration statement related to the common stock, or

enter into any swap or other agreement that transfers, in whole or in part, the economic consequence of ownership of any common stock whether any such swap or transaction is to be settled by delivery of shares or other securities, in cash or otherwise.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for or repayable with common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition.

New York Stock Exchange Listing

The shares are listed on the New York Stock Exchange under the symbol **PBYI**.

Price Stabilization, Short Positions

Until the distribution of the shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our common stock. However, the representatives may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with the offering, the underwriters may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. Covered short sales are sales made in an amount not greater than the underwriters

option to purchase additional shares described above. The underwriters may close out any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option granted to them. Naked short sales are sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the completion of the offering.

Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on the New York Stock Exchange, in the over-the-counter market or otherwise.

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Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor any of the underwriters make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Electronic Distribution

In connection with the offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

Some of the underwriters and their affiliates have engaged in, and may in the future engage in, investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. They have received, or may in the future receive, customary fees and commissions for these transactions.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area (each, a **Relevant Member State**), no offer of shares may be made to the public in that Relevant Member State other than:

- A. to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- B. 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 representatives; or
- C. in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares shall require us or the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person in a Relevant Member State who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed that it is a **qualified investor** within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive. In the case of any shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial

intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the representatives has been obtained to each such proposed offer or resale.

The Company, the representatives and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

This prospectus has been prepared on the basis that any offer of shares in any Relevant Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of shares. Accordingly any person making or intending to make an offer in that Relevant Member State of shares which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for the Company or any of the underwriters

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to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the Company nor the underwriters have authorized, nor do they authorize, the making of any offer of shares in circumstances in which an obligation arises for the Company or the underwriters to publish a prospectus for such offer.

For the purpose of the above provisions, the expression "an offer to the public" in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in the Relevant Member State by any measure implementing the Prospectus Directive in the Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC (including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member States) and includes any relevant implementing measure in the Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

Notice to Prospective Investors in the United Kingdom

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are "qualified investors" (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19 (5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, or the Order, and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons"). This document must not be acted on or relied on in the United Kingdom by persons who are not relevant persons. In the United Kingdom, any investment or investment activity to which this document relates is only available to, and will be engaged in with, relevant persons.

Notice to Prospective Investors in Switzerland

The shares 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 document 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 document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company or the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA (FINMA), and the offer of shares 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 shares.

Notice to Prospective Investors in the Dubai International Financial Centre

This prospectus supplement relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority, or DFSA. This prospectus supplement is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other

person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus supplement nor taken steps to verify the information set forth herein and has no responsibility for the prospectus supplement. The shares to which this prospectus supplement relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the shares offered should conduct their own due diligence on the shares. If you do not understand the contents of this prospectus supplement you should consult an authorized financial advisor.

Notice to Prospective Investors in Australia

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission (ASIC), in relation to the offering. This prospectus does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001 (the Corporations Act), and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the shares may only be made to persons (the Exempt Investors) who are sophisticated investors (within the meaning of section 708(8) of the Corporations Act), professional investors (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the shares without disclosure to investors under Chapter 6D of the Corporations Act.

The shares applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring shares must observe such Australian on-sale restrictions.

This prospectus contains general information only and does not take account of the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

Notice to Prospective Investors in Hong Kong

The shares have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to professional investors as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) 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 that Ordinance. No advertisement, invitation or document relating to the shares has been or may be issued or has been or may be in the possession of any person for the purposes of issue, 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 to do so under the securities laws of Hong Kong) other than with respect to shares 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 and any rules made under that Ordinance.

Notice to Prospective Investors in Japan

The shares have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) and, accordingly, will not be offered or sold, directly or indirectly, in Japan, or for the benefit of any Japanese Person or to others for re-offering or resale, directly or indirectly, in Japan or to any Japanese Person, except in compliance with all applicable laws, regulations and ministerial guidelines promulgated by relevant Japanese governmental or regulatory authorities in effect at the relevant time. For the purposes of this paragraph, Japanese Person shall mean any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

Notice to Prospective Investors in Singapore

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

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- (a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

- (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:
 - (a) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

 - (b) where no consideration is or will be given for the transfer;

 - (c) where the transfer is by operation of law;

 - (d) as specified in Section 276(7) of the SFA; or

 - (e) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

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LEGAL MATTERS

Legal matters in connection with the validity of the shares offered by this prospectus will be passed upon by Latham & Watkins LLP, Costa Mesa, California. Certain legal matters in connection with this offering will be passed upon for the underwriters by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts.

EXPERTS

The financial statements incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2012 have been so incorporated in reliance on the report of PKF Certified Public Accountants, A Professional Corporation, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

Available Information

We file reports, proxy statements and other documents with the SEC. You may read and copy any document we file at the SEC's public reference room at 100 F Street, N.E., Washington, D.C. 20549. You should call 1-800-SEC-0330 for more information on the public reference room. Our SEC filings are also available to you on the SEC's Internet website at <http://www.sec.gov>.

This prospectus is part of a registration statement that we filed with the SEC. The registration statement contains more information than this prospectus regarding us and our common stock, including certain exhibits and schedules. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC's Internet website.

Our Internet address is www.pumabiotechnology.com. The information on our Internet website is not incorporated by reference in this prospectus.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC permits us to incorporate into this prospectus information that we file with the SEC in other documents. This means that we can disclose important information to you by referring to other documents that contain that information. The information incorporated by reference is considered to be part of this prospectus. Information contained in this prospectus and information that we file with the SEC in the future and incorporate by reference in this prospectus automatically updates and supersedes previously filed information. We incorporate by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus and prior to the sale of all the shares covered by this prospectus or termination of the offering.

Our Annual Report on Form 10-K, filed with the SEC on April 1, 2013;

Our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 30, 2013;

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Our Quarterly Reports on Form 10-Q filed with the SEC on May 9, 2013, August 6, 2013 and November 12, 2013;

Our Current Reports on Form 8-K filed with the SEC on February 21, 2013, June 7, 2013, June 12, 2013, October 4, 2013, October 21, 2013, November 1, 2013, December 4, 2013 and December 26, 2013;
and

The description of our common stock contained in our Registration Statement on Form 8-A filed on October 16, 2012, and any subsequent amendment thereto filed for the purpose of updating such description. Also incorporated by reference into this prospectus are all documents that we may file with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the filing of this prospectus and prior to the termination of the offering of securities hereby. These documents include periodic reports, such

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as annual reports on Form 10-K and quarterly reports on Form 10-Q, and current reports on Form 8-K, as well as proxy statements. Any statement contained in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus. We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed above or filed in the future, that are not deemed filed with the SEC or any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or certain exhibits furnished pursuant to Item 9.01 of Form 8-K.

You may request a copy of these documents, including exhibits, which will be provided to you at no cost, by writing or telephoning us using the following contact information:

Puma Biotechnology, Inc.
10880 Wilshire Boulevard, Suite 2150
Los Angeles, California 90024
Attention: Investor Relations
Telephone: (424) 248-6500

You should rely only on the information contained in this prospectus or on information to which we have referred you. We have not authorized anyone else to provide you with any information.

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Shares

Puma Biotechnology, Inc.

Common Stock

PROSPECTUS

BofA Merrill Lynch

**Citigroup
, 2014**

Leerink Partners

Table of Contents**PART II****INFORMATION NOT REQUIRED IN PROSPECTUS****Item 14. *Other Expenses of Issuance and Distribution***

The following is an estimate of the expenses (all of which are to be paid by the registrant) that we may incur in connection with the securities being registered hereby.

| | |
|------------------------------|-------------|
| SEC registration fee | \$ 14,812 |
| FINRA filing fee | \$ 17,750 |
| Accounting fees and expenses | \$ * |
| Printing expenses | \$ * |
| Legal fees and expenses | \$ * |
| Miscellaneous | \$ * |
| Total | \$ * |

* To be completed by amendment.

Item 15. *Indemnification of Directors and Officers*

Subsection (a) of Section 145 of the General Corporation Law of the State of Delaware, or the DGCL, empowers a corporation to indemnify any person who was or is a party or who is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the corporation) by reason of the fact that the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with such action, suit or proceeding if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe the person's conduct was unlawful.

Subsection (b) of Section 145 empowers a corporation to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor by reason of the fact that the person acted in any of the capacities set forth above, against expenses (including attorneys fees) actually and reasonably incurred by the person in connection with the defense or settlement of such action or suit if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation, except that no indemnification shall be made in respect of any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of liability but in view of all the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

Section 145 further provides that to the extent a director or officer of a corporation has been successful on the merits or otherwise in the defense of any action, suit or proceeding referred to in subsections (a) and (b) of Section 145, or in defense of any claim, issue or matter therein, such person shall be indemnified against expenses (including attorneys fees) actually and reasonably incurred by such person in connection therewith; that indemnification provided for by Section 145 shall not be deemed exclusive of any other rights to which the indemnified party may be entitled; and the indemnification provided for by Section 145 shall, unless otherwise provided when authorized or ratified, continue as to a person who has ceased to be a director, officer, employee or agent and shall inure to the benefit of such person's heirs, executors and administrators. Section 145 also empowers the corporation to purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against any liability asserted against such person and incurred by such person in any such capacity, or arising out of his status as such, whether or not the corporation would have the power to indemnify such person against such liabilities under Section 145.

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Section 102(b)(7) of the DGCL provides that a corporation's certificate of incorporation may contain a provision eliminating or limiting the personal liability of a director to the corporation or its stockholders for monetary damages for breach of fiduciary duty as a director, provided that such provision shall not eliminate or limit the liability of a director (i) for any breach of the director's duty of loyalty to the corporation or its stockholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under Section 174 of the DGCL, or (iv) for any transaction from which the director derived an improper personal benefit.

Our amended and restated certificate of incorporation provides for indemnification of the officers and directors to the full extent permitted by applicable law. We have entered into indemnification agreements with each of our current directors and executive officers.

Item 16. Exhibits

(a) Exhibits

A list of exhibits filed with this registration statement on Form S-3 is set forth on the Exhibit Index and is incorporated herein by reference.

Item 17. Undertakings

(b) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(h) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

(i) The undersigned registrant hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

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Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement on Form S-3 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Los Angeles, State of California, on the 29th day of January, 2014.

PUMA BIOTECHNOLOGY, INC.

By: /s/ Alan H. Auerbach
 Alan H. Auerbach
 President and Chief Executive Officer

Each person whose signature appears below constitutes and appoints Alan H. Auerbach and Charles R. Eyler, and each of them singly, as his true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this registration statement and any and all additional registration statements pursuant to Rule 462(b) of the Securities Act of 1933, as amended, and to file the same, with all exhibits thereto, and all other documents in connection therewith, with the Securities and Exchange Commission, granting unto each said attorney-in-fact and agents, full power and authority to do and perform each and every act in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or either of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement on Form S-3 has been signed by the following persons in the capacities and as of the dates indicated.

| SIGNATURE | TITLE | DATE |
|--|--|------------------|
| /s/ Alan H. Auerbach Alan H. Auerbach | Chairman of the Board of Directors, President and Chief Executive Officer (Principal Executive Officer) | January 29, 2014 |
| /s/ Charles R. Eyler Charles R. Eyler | Senior Vice President, Finance and Administration and Treasurer (Principal Financial and Accounting Officer) | January 29, 2014 |
| /s/ Thomas R. Malley Thomas R. Malley | Director | January 29, 2014 |
| /s/ Jay M. Moyes Jay M. Moyes | Director | January 29, 2014 |
| /s/ Troy E. Wilson | Director | January 29, 2014 |

Troy E. Wilson

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| Number | Description |
|---------------|--|
| 1.1* | Form of Underwriting Agreement |
| 3.1 | Amended and Restated Certificate of Incorporation, as filed with the Secretary of State of the State of Delaware on November 14, 2011 (incorporated by reference to the Company's Information Statement on Schedule 14C filed on October 24, 2011) |
| 3.2 | Bylaws of Puma Biotechnology, Inc. (incorporated by reference to the Company's Annual Report on Form 10-SB filed on September 14, 2007) |
| 4.1 | Form of Common Stock Certificate (incorporated by reference to the Company's Post-Effective Amendment No. 1 to Form S-1 filed on March 30, 2012) |
| 5.1* | Opinion of Latham & Watkins LLP |
| 23.1* | Consent of Latham & Watkins LLP (included in Exhibit 5.1) |
| 23.2 | Consent of PKF Certified Public Accountants, A Professional Corporation, independent registered public accounting firm |
| 24.1 | Powers of Attorney (included on signature page) |

* To be filed by amendment.