

EPIX Pharmaceuticals, Inc.  
Form POS AM  
March 17, 2008

Table of Contents

As filed with the Securities and Exchange Commission on March 17, 2008

Registration No. 333-147800

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

POST-EFFECTIVE AMENDMENT NO. 1

TO  
Form S-1  
REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933

**EPIX PHARMACEUTICALS, INC.**

*(Exact Name of Registrant as Specified in Its Charter)*

**Delaware**  
*(State of Incorporation)*

**2835**  
*(Primary Standard Industrial  
Classification Code Number)*

**04-3030815**  
*(I.R.S. Employer  
Identification Number)*

**Four Maguire Road**  
**Lexington, Massachusetts 02421**  
**(781) 761-7600**  
*(Address, Including Zip Code, and Telephone Number,  
Including Area Code, of Registrant's Principal Executive Offices)*

**Michael G. Kauffman, M.D., Ph.D.**  
**Chief Executive Officer**  
**EPIX Pharmaceuticals, Inc.**  
**Four Maguire Road**  
**Lexington, Massachusetts 02421**  
**(781) 761-7600**  
*(Name, Address, Including Zip Code, and Telephone Number,  
Including Area Code, of Agent For Service)*

*Copy to:*

**Edward A. King, Esq.  
Goodwin Procter LLP  
Exchange Place  
53 State Street  
Boston, Massachusetts 02109  
(617) 570-1000**

**Approximate date of commencement of proposed sale to the public:** As soon as practicable after this registration statement becomes effective.

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, 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, 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 post-effective amendment filed pursuant to Rule 462(d) 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.

**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 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), shall determine.**

**This Registration Statement amends Amendment No. 1 to the Registration Statement on Form S-1 (No. 333-147800) of EPIX Pharmaceuticals, Inc. filed with the Commission on December 17, 2007. The shares registered hereby were originally registered on the Registration Statement on Form S-1 (No. 333-147800) of EPIX Pharmaceuticals, Inc. filed with the Commission on December 3, 2007. As a registration fee was paid on**

**the shares registered hereby in connection with their original registration, no registration fee is being paid in connection herewith.**

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**Table of Contents**

**EXPLANATORY NOTE**

This Post-Effective Amendment No. 1 to Form S-1 is being filed to incorporate by reference the Company's Annual Report on Form 10-K for the year ended December 31, 2007 into the Registration Statement on Form S-1 (No. 333-147800), and to make corresponding changes therein.

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**Table of Contents**

The information in this prospectus is not complete and may be changed. These securities may not be sold 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 offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

**SUBJECT TO COMPLETION, DATED MARCH 17, 2008**

**PROSPECTUS**

**5,245,468 Shares**

**Common Stock**

This prospectus relates to shares of common stock that may be sold by the selling stockholders identified in this prospectus. Specifically, this prospectus relates to the resale of 5,245,468 shares of our common stock. The selling stockholders acquired the shares offered by this prospectus in a private placement of our securities. We are registering the offer and sale of the shares to satisfy registration rights we have granted. We will not receive any of the proceeds from the sale of shares by the selling stockholders.

The selling stockholders may dispose of their shares of common stock or interests therein in a number of different ways and at varying prices. Please see Plan of Distribution.

Our common stock is listed on the NASDAQ Global Market under the symbol EPIX. On March 14, 2008, the last reported sale price of our common stock on the NASDAQ Global Market was \$2.85 per share.

**Investing in our common stock involves a high degree of risk. Before buying any shares, you should carefully read the discussion of material risks of investing in our common stock in Risk Factors beginning on page 3 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.**

You should rely only on the information contained in this prospectus or any prospectus supplement or amendment. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted.

The date of this prospectus is March 17, 2008.

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## TABLE OF CONTENTS

|  |    |
|--|----|
| <u>PROSPECTUS SUMMARY</u>                                | 1  |
| <u>RISK FACTORS</u>                                      | 3  |
| <u>SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</u> | 24 |
| <u>USE OF PROCEEDS</u>                                   | 25 |
| <u>SELLING STOCKHOLDERS</u>                              | 25 |
| <u>REGISTRATION RIGHTS</u>                               | 29 |
| <u>PLAN OF DISTRIBUTION</u>                              | 29 |
| <u>LEGAL MATTERS</u>                                     | 31 |
| <u>EXPERTS</u>   | 31 |
| <u>WHERE YOU CAN FIND MORE INFORMATION</u>               | 31 |
| <u>INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE</u>   | 31 |
| <u>Ex-23.1 Consent of Ernst &amp; Young LLP</u>          |    |

Unless the context otherwise requires, we use the terms EPIX, we, us and our in this prospectus to refer to EPIX Pharmaceuticals, Inc. and its subsidiaries. This prospectus contains trademarks, trade names, service marks and service names of EPIX and other companies.

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**Table of Contents**

**PROSPECTUS SUMMARY**

*This summary highlights selected information contained or incorporated by reference in this prospectus. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus carefully, including the risk factors, the financial statements and the documents incorporated herein by reference before making an investment decision.*

**Overview**

We are a biopharmaceutical company focused on discovering, developing and commercializing novel pharmaceutical products through the use of proprietary technology to better diagnose, treat and manage patients. We have four internally discovered therapeutic product candidates in clinical trials. These drug candidates are targeting conditions such as depression, Alzheimer's disease, cardiovascular disease and cognitive impairment. Our blood-pool imaging agent, Vasovist, is approved for marketing in more than 30 countries outside of the United States. We also have collaborations with SmithKline Beecham Corporation (GlaxoSmithKline), Amgen Inc., Cystic Fibrosis Foundation Therapeutics, Incorporated, and Bayer Schering Pharma AG, Germany. Our business strategy is to develop our internally discovered, novel pharmaceutical products through the point of proof of clinical concept, typically completion of Phase 2 clinical trials and then to seek pharmaceutical partnerships for the continued development, regulatory approvals and world-wide commercialization of the product candidates. In certain disease areas, such as pulmonary hypertension, where we believe we can efficiently obtain regulatory approval and effectively market the product through a specialty sales force, we may seek to retain commercialization rights in the United States.

The focus of our therapeutic drug discovery and development efforts is on the two classes of drug targets known as G-protein Coupled Receptors, or GPCRs, and ion channels. GPCRs and ion channels are classes of proteins embedded in the surface membrane of all cells and are responsible for mediating much of the biological signaling at the cellular level. We believe that our proprietary drug discovery technology and approach addresses many of the inefficiencies associated with traditional GPCR and ion channel-targeted drug discovery. By integrating computer-based, or in silico, technology with in-house medicinal chemistry, we believe that we can rapidly identify and optimize highly selective drug candidates. We focus on GPCR and ion channel drug targets whose role in disease has already been demonstrated in clinical trials or in preclinical studies. In each of our four clinical-stage therapeutic programs, we used our drug discovery technology and approach to optimize a lead compound into a clinical drug candidate in less than ten months, synthesizing fewer than 80 compounds per program. We moved each of these drug candidates into clinical trials in less than 18 months from lead identification. We believe our drug discovery technology and approach enables us to efficiently and cost-effectively discover and develop GPCR and ion channel-targeted drugs.

**Our Product Candidates**

The following chart summarizes the status of our therapeutic clinical drug development programs:



## **Table of Contents**

- \* Vasovist is approved for marketing in more than 30 countries outside of the United States. We have granted Bayer Schering Pharma AG, Germany an exclusive license to co-develop and market Vasovist worldwide. We are entitled to receive a royalty on products sold outside of the United States and, if Vasovist is approved and launched in the United States, a percentage of Bayer Schering Pharma AG, Germany's operating profit margin on products sold in the United States.

## **Risks Affecting Us**

You should carefully consider the matters discussed in the section **Risk Factors** beginning on page 3, including the following, before you invest in our stock. For example:

a substantial portion of our future revenues will be dependent upon our agreements with GlaxoSmithKline, Amgen Inc., Bayer Schering Pharma AG, Germany and other third-parties with whom we may in the future enter into a collaboration;

we anticipate future losses and may never become profitable; and

we have never had a commercially available product in the United States and we may never succeed in developing marketable products.

## **Recent Developments**

On November 15, 2007, we issued and sold in a private placement an aggregate of 5,245,468 shares of our common stock at a purchase price of \$3.10 per share. This private placement resulted in gross proceeds to us of approximately \$16.3 million, which, after payment of expenses of the private placement, will be used to finance ongoing clinical trials, advance our research and development activities and fund general corporate operations. In connection with the private placement, we have granted registration rights for the shares of our common stock received by the selling stockholders. See discussion of the registration rights discussed under the section **Registration Rights** on page 29.

## **Corporate Information**

We incorporated in Delaware in 1988 as Metacorp, Inc. and commenced operations in 1992. After changing our name to Metasyn Inc. in 1989 and EPIX Medical, Inc. in 1996, we changed our name to EPIX Pharmaceuticals, Inc. in 2004. Our principal executive offices are located at 4 Maguire Road, Lexington, Massachusetts 02421 and our telephone number is (781) 761-7600. Our website is located at <http://www.epixpharma.com>. Our Corporate Code of Conduct and Ethics as well as our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K and all amendments to these reports, which have been filed with the Securities and Exchange Commission, or SEC, are available to you free of charge through the Investor Relations section on our website as soon as reasonably practicable after such materials have been electronically filed with, or furnished to, the SEC. We do not intend for the other information contained in our website to be considered a part of this registration statement.

**Table of Contents**

**RISK FACTORS**

*Investing in our common stock involves a high degree of risk. You should carefully consider the following risk factors and the other information contained in this prospectus before making an investment decision. Additional risks and uncertainties not presently known to us, which we currently deem immaterial or which are similar to those faced by other companies in our industry or biomedical companies in general, may also impair our business operations. If any of these risks or uncertainties actually occurs, our business, financial condition or operating results could materially suffer. Please see *Special Note Regarding Forward-Looking Statements* and *Incorporation of Certain Documents by Reference*.*

**RISKS RELATED TO OUR BUSINESS**

*We anticipate future losses and may never become profitable.*

Our future financial results are uncertain. We have experienced significant losses since we commenced operations in 1992. Our accumulated net losses as of December 31, 2007 were approximately \$408.2 million. These losses have primarily resulted from expenses associated with our research and development activities, including preclinical studies and clinical trials, acquired in-process research and development from the merger with Predix and general and administrative expenses. We anticipate that our research and development expenses will remain significant in the future and we expect to incur losses over at least the next several years as we continue our research and development efforts, preclinical testing and clinical trials. In particular, we believe that we will be required to conduct additional clinical trials to obtain approval from the FDA for any of our therapeutic product candidates, which trials would be expensive and which could contribute to our continuing to incur losses.

As a result, we cannot predict when we will become profitable, if at all, and if we do, we may not remain profitable for any substantial period of time. If we fail to achieve profitability within the timeframe expected by investors, the market price of our common stock may decline and consequently our business may not be sustainable.

*We may need to raise additional funds necessary to fund our operations, and if we do not do so, we may not be able to implement our business plan.*

Since inception, we have funded our operations primarily through our public offerings of common stock, private sales of equity securities, debt financing, equipment lease financings, product development revenue, and royalty and license payments from our strategic partners. Although we believe that we have adequate funding to fund our operations through the first quarter of 2009, we may need to raise substantial additional funds for research, development and other expenses through equity or debt financings, strategic alliances or otherwise. Our future liquidity and capital requirements will depend upon numerous factors, including the following:

- the progress and scope of clinical trials;
- the timing and costs of filing future regulatory submissions;
- the timing and costs required to receive both U.S. and foreign governmental approvals;
- the cost of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights;
- the extent to which our product candidates gain market acceptance;

the timing and costs of product introductions;

the extent of our ongoing and any new research and development programs;

changes in our strategy or our planned activities;

**Table of Contents**

the costs of training physicians to become proficient with the use of our product candidates; and

the costs of developing marketing and distribution capabilities.

If we raise additional funds through the issuance of equity or convertible debt securities, the percentage ownership of our stockholders could be significantly diluted, and these newly issued securities may have rights, preferences or privileges senior to those of existing stockholders. If we incur additional debt financing, a substantial portion of our operating cash flow may be dedicated to the payment of principal and interest on such indebtedness, thus limiting funds available for our business activities. We cannot assure you that additional financing will be available on terms favorable to us, or at all. If adequate funds are not available or are not available on acceptable terms, when we desire them, our ability to fund our operations, take advantage of unanticipated opportunities or otherwise respond to competitive pressures would be significantly limited.

***We significantly increased our leverage as a result of the sale of 3.0% Convertible Senior Notes due 2024, and may be unable to repay, repurchase or redeem these notes if, and when, required.***

In connection with the sale of 3.0% Convertible Senior Notes due 2024, we have incurred indebtedness of \$100.0 million. Each \$1,000 of senior notes is convertible into 22.39 shares of our common stock representing a conversion price of approximately \$44.66 per share. Our ability to meet our debt service obligations will depend upon our future performance, which will be subject to regulatory approvals and sales of our products, as well as other financial and business factors affecting our operations, many of which are beyond our control. The amount of our indebtedness could, among other things:

make it difficult for us to make payments on the notes;

make it difficult for us to obtain financing for working capital, acquisitions or other purposes on favorable terms, if at all;

make us more vulnerable to industry downturns and competitive pressures; and

limit our flexibility in planning for, or reacting to changes in, our business.

In addition, although our 3.0% Convertible Senior Notes do not mature until 2024, noteholders may require us to repurchase these notes at par, plus accrued and unpaid interest, on June 15, 2011, 2014 and 2019 and upon certain other designated events under the notes, which include a change of control of us or termination of trading of our common stock on the NASDAQ Global Market. The definition of change in control set forth in the indenture governing the notes does not include certain mergers and similar transactions that are not deemed a change in control. While we believe that our merger with Predix did not constitute a change of control of us under the indenture, we cannot assure you that we will not become obligated to repurchase these notes, in whole or in part, as a result of the merger. Based on the current trading price of our common stock, we anticipate that in such event most, if not all, of the noteholders would tender their notes for repurchase. We may not have enough funds or be able to arrange for additional financing to repurchase the notes tendered by the holders upon a designated event or otherwise. Any failure to repurchase tendered notes would constitute an event of default under the indenture. If we are required to repurchase or redeem these notes prior to their maturity, whether as a result of the merger or otherwise, our financial position would be materially adversely affected and the anticipated benefits of the merger would be significantly diminished.

***A substantial portion of our future revenues will be dependent upon our agreements with GlaxoSmithKline, Amgen Inc. and Bayer Schering Pharma AG, Germany.***

We expect that a substantial portion of our future revenues will be dependent upon our collaboration agreements with GlaxoSmithKline and with Amgen Inc. The agreement with GlaxoSmithKline encompasses the development and commercialization of medicines targeting four G-protein coupled receptors, or GPCRs, for the treatment of a variety of diseases, including an option to license our 5-HT4 partial agonist, PRX-03140, and other medicines arising from the four research programs. The agreement with Amgen encompasses the development and commercialization of products based on our preclinical compounds that modulate the S1P1 receptor and compounds and products that may be identified by or acquired by Amgen and that

**Table of Contents**

modulate the S1P1 receptor. We are dependent upon Bayer Schering Pharma AG, Germany to commercialize Vasovist, our lead imaging product candidate, in the United States and Europe. If these collaborators were to terminate their agreements with us, fail to meet their obligations or otherwise decrease their commitment there under, our future revenues could be materially adversely affected and the development and commercialization of our product candidates would be interrupted. In addition, if we do not achieve some or any of the development, regulatory and commercial milestones or if GlaxoSmithKline or Amgen does not achieve certain net sales thresholds, in each case, as set forth in the respective agreements, we will not fully realize the expected benefits of the agreements. Further, the achievement of certain of the various milestones under our collaboration agreements with GlaxoSmithKline, Amgen and Bayer Schering Pharma AG, Germany will depend on factors that are outside of our control and most are not expected for several years, if at all. Moreover, our receipt of revenues under our agreements with these collaborators will be directly affected by the level of efforts of such collaborators and we cannot control whether they will devote sufficient resources to development or commercialization of the technology under their respective agreement or whether they will elect to pursue the development or commercialization of alternative products or services. For instance, Bayer Schering Pharma AG, Germany currently markets imaging agents for other technologies that will compete against Vasovist, and Bayer Schering Pharma AG, Germany will be responsible for setting the price of the product candidate worldwide. Accordingly, Bayer Schering Pharma AG, Germany may not set prices in a manner that maximizes revenues for us. Disagreements with our collaborators could delay or terminate the continued development and commercialization of the licensed products under our agreements or result in litigation, either of which could have a material adverse affect on our business, financial condition and results of operations overall. In addition, Bayer Schering Pharma AG, Germany was recently formed through the merger of Bayer AG and Schering AG. If the strategy of Bayer Schering Pharma AG, Germany differs from that of Schering AG's prior strategy with respect to the marketing of Vasovist, our expectations regarding the marketing of Vasovist could be negatively impacted, which could have a material adverse effect on our imaging business. If any of our agreements with GlaxoSmithKline, Amgen or Bayer Schering Pharma AG, Germany is terminated prior to expiration, we would be required to enter into other strategic relationships or find alternative ways of continuing our product development programs. We cannot assure you that we would be able to enter into similar agreements with other companies with sufficient product development capabilities to commercialize our product candidates, and our failure to do so could materially and adversely affect our ability to generate revenues.

***We have never had a commercially available product in the United States and we may never succeed in developing marketable products.***

We have never had any product candidates receive regulatory approval for commercial sale in the United States and do not expect to have any commercial therapeutic products available in the United States for at least the next several years, if at all. In September 2006, results from our pivotal Phase 3 clinical trial of our PRX-00023 product candidate for generalized anxiety disorder demonstrated that PRX-00023 did not achieve a statistically significant improvement over placebo for the primary endpoint with respect to generalized anxiety disorder. Prior to obtaining results from this trial, PRX-00023 was our most advanced therapeutic drug candidate. Based on these trial results, however, we have discontinued our development efforts with respect to PRX-00023 in anxiety and currently are focusing our development efforts for this product candidate in depression. Although we commenced a Phase 2b clinical trial of PRX-00023 for the treatment of depression in March 2007, PRX-00023 will require significant further testing for that indication. In addition, although our Vasovist imaging product has been approved for commercial sale, and is currently being marketed, in certain countries outside of the United States, we have not obtained approval of Vasovist in the United States and do not expect any significant income or royalties as a result of sales of Vasovist outside of the United States for the foreseeable future. The approval of Vasovist by the FDA is subject to continued uncertainty and we may never obtain regulatory approval to market Vasovist in the United States.

In addition to PRX-00023 and Vasovist, each of our other clinical-stage drug candidates in the United States require additional clinical studies: PRX-08066 for the treatment of two types of pulmonary hypertension    pulmonary

hypertension associated with chronic obstructive pulmonary disease and pulmonary arterial hypertension; PRX-03140 for the treatment of Alzheimer's disease; and PRX-07034 for the treatment

**Table of Contents**

of cognitive impairment. Prior to the initiation of our Phase 2 clinical trial, PRX-08066 had never been tested in patients with pulmonary hypertension associated with chronic obstructive pulmonary disease and has never been tested in patients with primary pulmonary arterial hypertension. PRX-07034 has only been tested in obese but otherwise healthy subjects and has never been tested in subjects with cognitive impairment. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in early-stage clinical development. For example, Sanofi-Aventis discontinued the development of its product candidate for the treatment of Alzheimer's disease designed to target the 5-HT4 protein receptor due to lack of efficacy. This compound is believed to have the same mechanism of action as PRX-03140, was more advanced in clinical development and was more potent in vitro assays. Accordingly, the results from the completed and ongoing studies and trials for our product candidates may not be predictive of the results we may obtain in later-stage clinical trials. If we are unable to develop one or more marketable products in the United States, or elsewhere, our results of operations, business and future prospects would be materially harmed.

***We have never generated positive cash flow, and if we fail to generate revenue, it will have a material adverse effect on our business.***

To date, we have received revenues from payments made under licensing, royalty arrangements and product development and marketing agreements with strategic collaborators. In particular, our revenue for the twelve months ended December 31, 2007 was \$14.9 million and consisted of \$10.2 million of product development revenue from Bayer Schering Pharma AG, Germany, GlaxoSmithKline and CFFT, \$1.0 million of royalty revenue related to the Bracco and Bayer Schering Pharma AG, Germany agreements, and \$3.7 million of license fee revenue related to the Bayer Schering Pharma AG, Germany, Amgen, Covidien, GlaxoSmithKline and CFFT agreements. In addition to these sources of revenue, we have financed our operations to date through public stock and debt offerings, private sales of equity securities and equipment lease financings.

Although we believe that we are currently in compliance with the terms of our collaboration and licensing agreements, the revenues derived from them are subject to fluctuation in timing and amount. We may not receive anticipated revenue under our existing collaboration or licensing agreements, these agreements may be subject to disputes and, additionally, these agreements may be terminated upon certain circumstances. Therefore, to achieve profitable and sustainable operations, we, alone or with others, must successfully develop, obtain regulatory approval for, introduce, market and sell products. We may not receive revenue from the sale of any of our product candidates for the next several years because we, and our partners, may not:

- successfully complete our product development efforts;
- obtain required regulatory approvals in a timely manner, if at all;
- manufacture our product candidates at an acceptable cost and with acceptable quality; or
- successfully market any approved products.

As a result, we may never generate revenues from sales of our product candidates and our failure to generate positive cash flow could cause our business to fail.

***We depend on our strategic collaborators for support in product development and the regulatory approval process for our product candidates and, if approved, for product marketing.***

Our product development programs and potential regulatory approval and commercialization of our product candidates will require substantial additional cash to fund expenses. Our strategy includes collaborating with leading



pharmaceutical, biotechnology or other companies to assist us in further developing and potentially commercializing our product candidates requiring large commercial sales and marketing infrastructures. We may also seek to enter into such collaborations for our other product candidates, especially for target indications in which the potential collaborator has particular expertise or that involve a large, primary care market that must be served by large sales and marketing organizations. In addition, we depend, and expect to continue to depend, on strategic collaborators for support in a variety of other activities including manufacturing, marketing and distribution of our product candidates in the United States and abroad, if the FDA and corresponding foreign

## **Table of Contents**

agencies approve our product candidates for marketing. We face significant competition in seeking appropriate collaborators and these collaborations are complex and time-consuming to negotiate and document.

We may not be able to enter into any such collaboration on terms that are acceptable to us, or at all. If that were to occur, we may have to curtail the development of a particular product candidate, reduce or delay one or more of our development programs or potential commercialization, or increase our expenditures and undertake development or commercialization activities at our own expense. For instance, on July 12, 2006, Bayer Schering Pharma AG, Germany notified us that it decided not to exercise its option to exclusively license EP-2104R, our imaging agent that has completed a Phase 2 clinical trial. As a result, we discontinued the development of EP-2104R. If we elect to increase our expenditures to fund development, potential regulatory approval or commercialization activities on our own, we will need to obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not obtain sufficient funds, we will not be able to complete clinical development of our product candidates or bring our product candidates to market. Further, our receipt of revenues from strategic alliances is affected by the level of efforts of our collaborators. Our collaborators may not devote the resources necessary to complete development and commence marketing of a product candidate in their respective territories, or they may not successfully market product candidates.

***We rely on third-parties to conduct our clinical trials, and those third-parties may not perform satisfactorily, including failing to maintain adequate diligence in the conduct of our trials and failing to meet established deadlines for the completion of such trials.***

We do not have the ability to independently conduct clinical trials for our product candidates, and we rely on third-parties such as contract research organizations, medical institutions and clinical investigators to enroll qualified patients and conduct our clinical trials. Our reliance on these third-parties for clinical development activities reduces our control over these activities. Accordingly, these third-party contractors may not complete activities on schedule, or may not conduct our clinical trials in accordance with regulatory requirements or our trial design. Our reliance on third-parties that we do not control does not relieve us of our requirement to prepare, and ensure our compliance with, various procedures required under good clinical practices, even though third-party contract research organizations have prepared and are complying with their own, comparable procedures. If these third-parties do not successfully carry out their contractual duties or regulatory obligations or meet expected deadlines, if the third-parties need to be replaced or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our preclinical development activities or clinical trials may be extended, delayed, suspended or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize, our product candidates. In addition, if our contract research organizations and other similar entities with which we are working do not successfully carry out their contractual duties or meet expected deadlines, we may be required to replace them. For example, in January 2008, we had to cease doing business with one of our third-party contract research organizations as a result of errors in the trial results from our Phase 2a clinical trial of PRX-03140 which were provided by such third-party and publicly reported by us. Although we believe that there are other third-party contractors we could engage to continue these activities, it may result in a delay of the affected trial. In addition, our failure to accurately report study data, whether as a result of a failure by a third-party or otherwise, could harm our reputation and subject us to liability.

***If clinical trials for our product candidates are prolonged or delayed, we may be unable to commercialize our product candidates on a timely basis, which would require us to incur additional costs and delay our receipt of any revenue from potential product sales.***

We may encounter problems with our completed, ongoing or planned clinical trials for our product candidates that will cause us or any regulatory authority to delay or suspend those clinical trials or delay the analysis of data derived from them. A number of events, including any of the following, could delay the completion of our ongoing and

planned clinical trials for our product candidates and negatively impact our

**Table of Contents**

ability to obtain regulatory approval or enter into collaborations for, or market or sell, a particular product candidate, including any of our current clinical-stage product candidates:

conditions imposed on us by the FDA or any foreign regulatory authority regarding the scope or design of our clinical trials;

delays in obtaining, or our inability to obtain, required approvals from institutional review boards or other reviewing entities at clinical sites selected for participation in our clinical trials;

delay in developing a clinical dosage form, insufficient supply or deficient quality of our product candidates or other materials necessary to conduct our clinical trials;

negative or inconclusive results from clinical trials, or results that are inconsistent with earlier results, that necessitate additional clinical study;

serious and/or unexpected product-related side effects experienced by subjects in clinical trials; or

failure of our third-party contractors or our investigators to comply with regulatory requirements or otherwise meet their contractual obligations to us in a timely manner.

Regulatory authorities, clinical investigators, institutional review boards, data safety monitoring boards and the hospitals at which our clinical trials are conducted all have the power to stop our clinical trials prior to completion. Our clinical trials for our product candidates may not begin as planned, may need to be restructured, and may not be completed on schedule, if at all. For example, in September 2001, after discussions with the FDA, we expanded our initial target indication for Vasovist from one specific body region, the aortoiliac region, to a broader indication that included the entire body's vascular system, except for the heart. This expansion required us to add two new clinical trials to our then existing Phase 3 clinical trial program. This change to the Phase 3 clinical trial program and the associated delay in the startup of new clinical centers resulted in an approximate 15-month delay in our NDA submission and an increase in costs associated with the program. Delays in clinical trials may result in increased development costs for our product candidates. In addition, if our clinical trials for our product candidates are delayed, our competitors may be able to bring product candidates to market before we do and the commercial viability of our product candidates could be significantly reduced.

In addition, the number and complexity of clinical trials needed to achieve regulatory approval for our therapeutic drug candidates, including but not limited to PRX-00023, our product candidate for the treatment of depression, and PRX-03140, our product candidate for the treatment of Alzheimer's disease, could be significant. Achieving primary efficacy endpoints in depression and anxiety trials is difficult due to the significant placebo effect commonly observed in trials in these patient populations. For example, results from our completed Phase 3 clinical trial of PRX-00023 demonstrated that the product candidate did not achieve a statistically significant improvement over placebo for the primary endpoint with respect to generalized anxiety disorder. Based on these results, we have discontinued our development efforts with respect to PRX-00023 in anxiety and are focusing our efforts with respect to PRX-00023 in depression. In addition, we must also submit the results of a two-year carcinogenicity study of PRX-00023 prior to its approval. We have not yet initiated this study and intend to conduct this study prior to submitting an NDA to the FDA. If the clinical development of PRX-00023 is delayed as a result of these matters, additional requirements set forth by the FDA, including requirements related to confirming the correct dose for PRX-00023, or otherwise, the time and cost of the development of PRX-00023 could increase significantly.

***If we are unsuccessful in our appeal process for Vasovist with the FDA, we may never obtain approval to market and sell Vasovist in the United States and our revenues will be materially harmed.***

Vasovist has not been approved for marketing and sale in the United States by the FDA. In connection with a new drug application, or NDA, that we submitted for Vasovist in December 2003, we received an approvable letter from the FDA in January 2005 in which the FDA requested additional clinical trials prior to approval. In May 2005, we submitted a response to the FDA approvable letter, which was accepted by the FDA as a complete response in June 2005. In November 2005, the FDA provided us with a second approvable

**Table of Contents**

letter which indicated that at least one additional clinical trial and a re-read of images obtained in certain previously completed Phase 3 trials will be necessary before the FDA could approve Vasovist. After considering the parameters of the additional clinical trials requested by the FDA, we filed a formal appeal with the FDA asking the FDA to approve Vasovist and to utilize an advisory committee as part of the appeal process. In August 2006, the FDA denied our appeal and suggested that we conduct two new clinical trials for Vasovist. In February 2007, we filed our second formal appeal with the FDA asking the FDA to approve Vasovist and to utilize an advisory committee as part of the appeal process. On June 15, 2007, we received a letter from the FDA denying our second formal appeal, but indicated that a blinded re-read, or reanalysis, of the images obtained in our previously completed Phase 3 clinical trials of Vasovist could provide the potential evidence to support approval of Vasovist if the results of the re-read are positive. In January 2008, we initiated the re-read of the images obtained in prior Phase 3 studies. The approval, timeliness of approval and labeling of Vasovist, however, remain subject to significant uncertainties related to a number of factors, including:

obtaining positive results of such a re-read of images by a new group of radiologists; and

the FDA's review process and conclusions regarding any additional Vasovist regulatory submissions.

We cannot assure you that the blinded re-read process will be successful or that the FDA will approve Vasovist upon the resubmission of the NDA if the re-read is successful. If the FDA does not approve Vasovist, we will not receive revenues based on sales of Vasovist in the United States.

***If we are unable to obtain required regulatory approval of our therapeutic product candidates, we will be unable to market and sell our therapeutic product candidates and our business will be materially harmed.***

Our existing therapeutic product candidates and any other product candidates we may discover or acquire and seek to commercialize are subject to extensive regulation by the FDA and similar regulatory agencies in other countries relating to development, clinical trials, manufacturing and commercialization. In the United States and in many foreign jurisdictions, rigorous preclinical testing and clinical trials and an extensive regulatory review process must be successfully completed before a new product candidate can be sold. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. The time required to obtain approval by the FDA is unpredictable but typically exceeds five years following the commencement of clinical trials, depending upon many factors, including the complexity of the product candidate. We initiated clinical trials for PRX-08066, PRX-00023, PRX-03140 and PRX-07034 in May 2005, February 2004, December 2004 and June 2006, respectively, and thus far, these therapeutic product candidates have been studied in only a small number of patients. Early-stage clinical trials in small numbers of patients are often not predictive of results in later-stage clinical trials with a larger and more diverse patient population. Even product candidates with favorable results in late-stage pivotal clinical trials may fail to get approved for commercialization for many reasons, including:

our failure to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for a particular indication;

our inability to demonstrate that a product candidate's benefits outweigh its risks;

our inability to demonstrate that the product candidate presents a significant advantage over existing therapies;

the FDA's or comparable foreign regulatory authorities' disagreement with the manner in which we and our collaborators interpret the data from preclinical studies or clinical trials;

the FDA's or comparable foreign regulatory authorities' failure to approve our manufacturing processes or facilities or the processes or facilities of our collaborators; or

a change in the approval policies or regulations of the FDA or comparable foreign regulatory authorities.

The relevant regulatory authorities may not approve any of our applications for marketing authorization relating to any of our product candidates, or additional applications for or variations to marketing

**Table of Contents**

authorizations that we may make in the future as to these or other product candidates. Among other things, we have had only limited experience in preparing applications and obtaining regulatory approvals. If approval is granted, it may be subject to limitations on the indicated uses for which the product candidate may be marketed or contain requirements for costly post-marketing testing and surveillance to monitor safety or efficacy of the product candidate. If approval of an application to market product candidates is not granted on a timely basis or at all, or if we are unable to maintain our approval, our business may be materially harmed. It is possible that none of our product candidates or any other product candidates we may seek to develop in the future will ever obtain the appropriate regulatory approvals necessary for us to begin selling them, which would materially harm our business.

***Our clinical trials may not yield results that will enable us to obtain regulatory approval for our product candidates.***

We will only receive regulatory approval to commercialize a product candidate if we can demonstrate to the satisfaction of the FDA or the applicable foreign regulatory agency, in well-designed and conducted clinical trials, that the product candidate is safe and effective and otherwise meets the appropriate standards required for approval for a particular indication. Clinical trials are lengthy, complex and extremely expensive processes with uncertain results. For example, results from our completed Phase 3 clinical trial of PRX-00023 in generalized anxiety disorder, which was designed to evaluate the efficacy of PRX-00023 as measured by the change from baseline in the Hamilton Rating Scale for Anxiety compared to placebo, demonstrated that PRX-00023 did not achieve a statistically significant improvement over placebo for the primary endpoint with respect to generalized anxiety disorder. Based on these results, we have discontinued our development efforts of PRX-00023 in anxiety. We have limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals for our product candidates, including filing and prosecuting the applications necessary to gain approval by the FDA. Our NDA for Vasovist has not been, and may never be, approved by the FDA and we have not submitted an NDA to the FDA for any of our other product candidates. This limited experience may result in longer regulatory processes in connection with our efforts to obtain approval of our product candidates. With respect to both our current product candidates in human clinical trials and our research product candidates which may be suitable for testing in human clinical trials at some point in the future, we face risks including that:

the product candidate may not prove to be safe and efficacious;

the dosage form of the product candidate may not deliver reproducible amounts of product to patients;

patients may die or suffer other adverse effects for reasons that may or may not be related to the product candidate being tested;

the results of later-stage clinical trials may not confirm the positive results of earlier trials;

the results may not meet the level of statistical significance required by the FDA or other regulatory agencies for approval; and

the FDA or other regulatory agencies may require additional or expanded trials.

Of the large number of product candidates in development, only a small percentage result in the submission of an NDA to the FDA and even fewer are approved for commercialization. If we fail to demonstrate the safety and efficacy of our product candidates, we will not be able to obtain the required regulatory approvals to commercialize these product candidates. The results from preclinical testing of a product candidate that is under development may not be predictive of results that will be obtained in human clinical trials. In addition, the results of early human clinical trials may not be predictive of results that will be obtained in larger scale, advanced-stage clinical trials. Our current product



candidates and any other product candidates we may seek to develop in the future may never complete the clinical testing necessary to obtain the appropriate regulatory approvals for us to begin selling them.

**Table of Contents**

***Gadolinium-based imaging agents, such as Vasovist, may cause adverse side effects which could limit our ability to receive approval for these product candidates and our ability to effectively market these product candidates, if approved.***

Vasovist is a contrast drug that contains gadolinium. In May 2006, the Danish Medicines Agency announced that it was investigating a possible link between the use of Omniscan, an imaging agent containing gadolinium, and the development of a very rare skin disease, nephrogenic systemic fibrosis (NSF), in 25 patients with severely impaired renal function who had been administered the imaging agent. Further investigations with respect to all MRI contrast media containing gadolinium revealed that NSF also has developed following the administration of two other gadolinium-containing agents (OptiMARK and Magnevist). It also has been reported that NSF may affect internal anatomy as well as the skin. Although a causative relationship between gadolinium-containing agents and NSF has not been definitively established, evidence is increasing. By May 2007, the use of Omniscan and Magnevist had been contraindicated in patients with severe renal impairment by the EMEA (European Medicines Agency). For all other gadolinium-containing contrast agents, safety warnings about the potential for NSF in patients with severe renal impairment were added to the product information. By May 2007, the FDA requested that manufacturers of all gadolinium-containing agents add a Boxed Warning and new Warning section that describes the risk of NSF because it is impossible at present to definitively determine whether the extent of risks for developing NSF are the same for all gadolinium-containing agents. We are also aware of ongoing litigation in the United States relating to the use of imaging agents containing gadolinium. To date, over 250 cases of NSF have been reported world-wide. Although we have reviewed our safety databases for Vasovist and have found no instances of this rare disease, our databases may be too small to show such an effect, if it exists. In the event gadolinium-based imaging agents such as Vasovist are directly linked to this very rare disease or other unanticipated side effects, such safety concerns could have a material adverse effect on our ability to obtain marketing approval for Vasovist or any such approval for use may be revoked. Moreover, even if a direct link is not conclusively established, any safety concerns regarding gadolinium-based imaging agents could also materially harm our and our partners' ability to successfully market Vasovist.

***If we encounter difficulties enrolling subjects in our clinical trials for our product candidates, or subjects drop out of trials in progress for our product candidates, our trials could be delayed or otherwise adversely affected.***

The timing of completion of clinical trials is dependent in part upon the rate of enrollment of patients. Patient accrual is a function of many factors, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the existence of competitive clinical trials, and the availability of alternative treatments. Delays in planned patient enrollment may result in increased costs and prolonged clinical development. In addition, patients may withdraw from a clinical trial for a variety of reasons. If we fail to accrue and maintain the number of patients into one of our clinical trials for which the clinical trial was designed, the statistical power of that clinical trial may be reduced which would make it harder to demonstrate that the product candidate being tested in such clinical trial are safe and effective. We may not be able to enroll a sufficient number of qualified patients in a timely or cost-effective manner. For example, we experienced difficulty in enrolling healthy elderly volunteers in our Phase 1 clinical trial for PRX-03140. Any future delays in patient enrollment could result in increased costs and longer development times. Enrollment of patients in our clinical trials for our product candidates is affected by many factors, including:

the limited size of the patient population and the availability of commercial products for certain target indications, including pulmonary arterial hypertension and pulmonary hypertension associated with chronic obstructive pulmonary disease;

the nature and design of the trial protocol;

the proximity of patients to clinical sites;

the availability of other effective treatments for the relevant disease (whether approved or experimental);

**Table of Contents**

the eligibility criteria for enrollment in our clinical trials;

perceived risks and benefits of the product candidate under study; and

competing studies or trials.

In addition, the FDA could require us to conduct clinical trials with a larger number of subjects than we have projected for any of our product candidates. If we have difficulty enrolling or retaining a sufficient number of patients to participate and complete our clinical trials for our product candidates as planned, we may need to delay or terminate ongoing or planned clinical trials. Delays in enrolling patients in these clinical trials or the withdrawal of subjects enrolled in these clinical trials would adversely affect our ability to develop and seek approval for our product candidates, could delay or eliminate our ability to generate product candidates and revenue and could impose significant additional costs on us.

***Our therapeutic product candidates are currently unformulated.***

All of our therapeutic product candidates, including PRX-08066, PRX-00023, PRX-03140 and PRX-07034, are currently unformulated. The lack of an optimized and commercially-viable formulation during clinical trials may have a significant impact in the overall development and commercialization of these therapeutic product candidates, including:

the current dosage may not provide reproducible amounts of product;

the pharmaceutical development of a commercially viable formulation may add significant cost and time to our clinical development programs for therapeutics;

additional trials may be required if the new formulation is not bioequivalent to formulations already used in clinical trials;

future clinical trials may be delayed in order to identify, develop, optimize, manufacture and certify a commercially viable formulation; and

regulatory filings, and/or commercial launch may be delayed due to the lack of a commercial process for cGMP manufacturing of the new formulation.

The occurrence of any of the foregoing could materially harm our business.

***Our prior stock option practices may result in significant liability.***

Prior to the change in our senior management in connection with the merger with Predix Pharmaceuticals Holdings, Inc. on August 16, 2006, certain employees, including certain of our former senior management, participated in retrospective date selection for the grant of certain stock options and re-priced, as defined by financial accounting standards, certain options during the period from 1997 through 2005. Accordingly, our audit committee concluded that, pursuant to Accounting Principles Board No. 25 (APB 25) and related interpretations, the accounting measurement date for the stock option grants for which those members of our former senior management had retrospectively selected grant dates for certain grants awarded between February 1997 and February 2004, covering options to purchase approximately 1.4 million shares of our common stock, differed from the measurement dates previously used for such stock awards. In addition, we determined that certain of our former senior management

re-priced, as defined by financial accounting standards, approximately 0.9 million stock options awarded during the period between June 1999 and March 2005, and we identified approximately 0.1 million options in which other dating errors resulted in stock options with grant dates that failed to meet the measurement date criteria of APB 25. As a result, we applied revised measurement dates to the option grants with administrative errors and option grants for which certain of our former senior management retrospectively selected grant dates, and, for options that were re-priced, as defined by financial accounting standards, we revised our accounting for such re-priced awards from accounting for the grants as fixed awards to accounting for the grants as variable awards. As a result of these adjustments, in connection with the filing of our 2006 Form 10-K, we restated our historical financial statements for the years 1997 through 2005 to record an aggregate of \$7.4 million in additional stock-based

## **Table of Contents**

compensation expense for those periods. In addition, we accrued payroll tax expense of approximately \$0.9 million relating to employer and employee payroll taxes, interest and penalties we estimate we will owe as a result of the modifications to exercised options previously considered incentive stock options that should have been taxed as non-qualified stock options. Our historical stock option practices and the restatement of our prior financial statements expose us to greater risks associated with litigation and regulatory proceedings. The Securities and Exchange Commission has advised us that it has commenced an informal investigation regarding our stock option grants. We are cooperating with that investigation. In the event of any litigation or regulatory proceeding involving a finding or assertion by the Securities and Exchange Commission, other federal or state governmental agencies, or any third-party that our past stock option practices violated the federal securities laws or other laws, we may be required to pay fines, penalties or other amounts, may be subject to other remedies or remedial actions, and/or may be required to further restate prior period financial statements or adjust current period financial statements. In addition, considerable legal and accounting expenses related to these matters have been incurred to date and significant expenditures may be incurred in the future.

***Failure to comply with foreign regulatory requirements governing human clinical trials and marketing approval for our product candidates could prevent us from selling our product candidates in foreign markets, which may adversely affect our operating results and financial condition.***

The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement for marketing our product candidates outside the United States vary greatly from country to country and may require additional testing. We have no experience in obtaining regulatory approvals for any of our product candidates. Although the use of Vasovist has been approved in the European Union, as well as Canada, Iceland, Norway, Switzerland, Turkey and Australia, Bayer Schering Pharma AG, Germany is responsible for obtaining foreign regulatory approvals for Vasovist. The time required to obtain approvals outside the United States may differ from that required to obtain FDA approval. We may not obtain foreign regulatory approvals on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other countries or by the FDA. Failure to comply with these regulatory requirements or obtain required approvals could impair our ability to develop foreign markets for our product candidates.

***Our product candidates will remain subject to ongoing regulatory requirements even if they receive marketing approval, and if we fail to comply with requirements, we could lose these approvals and the sale of any approved commercial products could be temporarily or permanently suspended.***

Even if we receive regulatory approval to market a particular product candidate, the product will remain subject to extensive regulatory requirements, including requirements relating to manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion and record keeping. In addition, as clinical experience with a product expands after approval because it is typically used by a greater number of patients after approval than during clinical trials, side effects and other problems may be observed after approval that were not seen or anticipated during pre-approval clinical trials. We are required to maintain pharmacovigilance systems for collecting and reporting information concerning suspected adverse reactions to our product candidates. In response to pharmacovigilance reports, regulatory authorities may initiate proceedings to revise the prescribing information for our product candidates or to suspend or revoke our marketing authorizations. Procedural safeguards are often limited, and marketing authorizations can be suspended with little or no advance notice. Both before and after approval of a product, quality control and manufacturing procedures must conform to cGMP. Regulatory authorities, including the European Medicines Agency, or EMEA, and the FDA, periodically inspect manufacturing facilities to assess compliance with cGMP. Accordingly, we and our contract manufacturers will need to continue to expend time, funds, and effort in the area of production and quality control to maintain cGMP compliance. If we fail to comply with the regulatory requirements of the FDA, the EMEA and other applicable U.S. and foreign regulatory authorities or

previously unknown problems

**Table of Contents**

with any approved commercial products, manufacturers or manufacturing processes are discovered, we could be subject to administrative or judicially imposed sanctions or other setbacks, including:

restrictions on the products, manufacturers or manufacturing processes;

warning letters;

civil or criminal penalties;

fines;

injunctions;

product seizures or detentions;

import bans;

product recalls and related publicity requirements;

unanticipated expenditures;

total or partial suspension of production; and

refusal to approve pending applications for marketing approval of new products or supplements to approved applications.

The imposition on us of any of the foregoing could materially harm our results of operations. In addition to regulations adopted by the EMEA, the FDA, and other foreign regulatory authorities, we are also subject to regulation under the Occupational Safety and Health Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act, and other federal, state, and local regulations.

***We are focusing our therapeutic product discovery and development efforts on G-Protein Coupled Receptor and ion channel-targeted product candidates, which have historically had a high incidence of adverse side effects.***

Despite commercial success, many G-Protein Coupled Receptor, or GPCR, and ion channel-targeted products have been associated with a high incidence of adverse side effects due in part to poor selectivity in binding to their target protein, resulting in binding to other off-target proteins. We believe we are designing our therapeutic product candidates to be highly selective and as a result to have a favorable side-effect profile. However, all of our therapeutic product candidates are in early stages of development, and although our clinical therapeutic product candidates have to date exhibited acceptable side-effect profiles in clinical trials in a limited number of subjects, we cannot assure you that these results will be repeated in larger-scale trials. If serious side effects occur in later-stage clinical trials of our therapeutic product candidates, we may not receive regulatory approval to commercialize them. Even if any of our therapeutic product candidates receive regulatory approval, if they do not exhibit a more favorable side-effect profile than existing therapies, our competitive position could be substantially diminished.

***The application of our in silico therapeutic product discovery technology and approach may be limited to a subset of therapeutically useful proteins, which may reduce the opportunities to develop and commercialize product candidates against other important therapeutic targets.***



To date, our technology and approach has generated clinical therapeutic product candidates, including PRX-08066, PRX-00023, PRX-03140 and PRX-07034, which mimic the activity of a small molecule, serotonin, within a class of GPCR proteins known as serotonergic receptors. The activity is achieved through binding of the ligand, serotonin, to a particular region of the protein that spans the cell membrane. These GPCRs and mechanisms of interaction represent a small subset of all known therapeutically-relevant GPCRs. Ion channels can consist of multiple protein subunits that have complex and subtle mechanisms of activation and inactivation. Therefore, it may be difficult to apply our proprietary product discovery technology to small-molecule ion channel targets.

**Table of Contents**

Although we believe that the in silico technology platform can be utilized and developed to discover such small molecules, we cannot ensure that our in silico technology and approach will generate clinical candidates for all GPCRs and ion channels that are important targets for therapeutic intervention.

***Our competitors may develop products that are less expensive, safer or more effective, which may diminish or eliminate the commercial success of any future products that we may commercialize.***

Competition in the pharmaceutical and biotechnology industries is intense and expected to increase. We face competition from pharmaceutical and biotechnology companies, as well as numerous academic and research institutions and governmental agencies engaged in product discovery activities or funding, both in the United States and abroad. Some of these competitors have therapeutic products or are pursuing the development of therapeutic product candidates that target the same diseases and conditions that are the focus of our clinical-stage therapeutic product candidates, including the following:

*PRX-00023.* If approved, PRX-00023, the product candidate we are developing for the treatment of depression, may compete with approved products from such pharmaceutical companies as Forest Laboratories, Inc., GlaxoSmithKline plc, Eli Lilly & Co., Pfizer Inc. and Wyeth, and may compete with several therapeutic product candidates in clinical development from other companies, including Sanofi-Aventis. We believe that there are over 60 therapeutic product candidates in clinical trials or that have been submitted for approval for the treatment of depression.

*PRX-03140.* If approved, PRX-03140, the drug candidate we are developing for the treatment of Alzheimer's disease, may compete with approved products from such pharmaceutical companies as Forest Laboratories, Inc., Johnson & Johnson, Novartis AG and Pfizer, Inc., and may compete with drug candidates in clinical development from other companies, including Myriad Genetics, Inc., GlaxoSmithKline plc and Neurochem Inc. We are studying PRX-03140 both as monotherapy and in combination with approved products, such as Aricept which is marketed by Pfizer Inc. We believe that there are over 70 therapeutic product candidates in clinical trials for the treatment of Alzheimer's disease.

*PRX-08066.* If approved, PRX-08066, the drug candidate we are developing for the treatment of pulmonary arterial hypertension (PAH), may compete with approved products from such pharmaceutical companies as Actelion Pharmaceuticals Ltd., GlaxoSmithKline plc, Pfizer Inc., Gilead Sciences Inc., and United Therapeutics Corporation, and may compete with drug candidates in clinical development by other companies, such as Encysive Pharmaceuticals Inc. and Bayer Schering Pharma AG. We believe that there are approximately ten therapeutic product candidates in clinical trials or that have been submitted for approval for the treatment of pulmonary arterial hypertension and/or pulmonary hypertension associated with chronic obstructive pulmonary disease.

*PRX-07034.* If approved for the treatment of cognitive impairment (associated with schizophrenia or Alzheimer's disease), PRX-07034 may compete with approved products from such pharmaceutical companies as Forest Laboratories, Johnson & Johnson, Novartis AG and Pfizer, Inc., and may compete with several therapeutic product candidates in clinical development from other companies, including GlaxoSmithKline plc, AstraZeneca and Memory Pharmaceuticals Corp. We believe that there are over 60 therapeutic product candidates in clinical trials for the treatment of cognitive impairment in association with schizophrenia. If approved for the treatment of obesity, PRX-07034 may compete with approved products from such pharmaceutical companies as Abbott Laboratories and Roche Holding Ltd., and may compete with several therapeutic product candidates in clinical development by other companies, such as Sanofi-Aventis and Arena Pharmaceuticals, Inc. We believe that there are over 40 therapeutic product candidates in clinical trials for the

treatment of obesity.

We expect that many patents covering commercial therapeutic products for these indications will expire in the next four to nine years, which will result in greater competition in these indications resulting from companies producing generic versions of the commercial products. Many of our competitors have therapeutic products that have been approved or are in advanced development and may develop superior technologies or methods to identify and validate therapeutic product targets and to discover novel small-molecule products.

## **Table of Contents**

Our competitors may also develop alternative therapies that could further limit the market for any therapeutic products that we may develop.

In addition, there are a number of general use MRI agents approved for marketing in the United States, and in certain foreign markets that, if used or developed for magnetic resonance angiography, are likely to compete with Vasovist. Such products include Magnevist and Gadovist by Bayer Schering Pharma AG, Germany, Dotarem by Guerbet, S.A., Omniscan by GE Healthcare, ProHance and MultiHance by Bracco and OptiMARK by Covidien Ltd. We are aware of five agents under clinical development that have been or are being evaluated for use in magnetic resonance angiography: Bayer Schering Pharma AG, Germany's Gadomer and SHU555C, Guerbet, S.A.'s Vistarem, Bracco's B-22956/1, Ferropharm GmbH's Code VSOP-C184, and Advanced Magnetics Inc. Ferumoxytol. Moreover, there are several well-established medical imaging methods that currently compete and will continue to compete with MRI, including digital subtraction angiography, which is an improved form of X-ray angiography, computed tomography angiography, nuclear medicine and ultrasound, and there are companies that are actively developing the capabilities of these competing methods to enhance their effectiveness in vascular system imaging.

We cannot assure you that our competitors will not succeed in the future in developing therapeutic or imaging products that are more effective than any that we are developing. We believe that our ability to compete in developing commercial products depends on a number of factors, including the success and timeliness with which we complete FDA trials, the breadth of applications, if any, for which our product candidates receive approval, and the effectiveness, cost, safety and ease of use of our product candidates in comparison to the products of our competitors. In addition, these companies may be more successful than we are in developing, manufacturing and marketing their imaging products. In addition, many of our competitors and their collaborators have substantially greater capital, research and development resources, manufacturing, sales and marketing experience and capabilities. Smaller companies also may prove to be significant competitors, particularly through proprietary research discoveries and collaboration arrangements with large pharmaceutical and established biotechnology companies. Our competitors, either alone or with their collaborators, may succeed in developing products that are more effective, safer, more affordable or more easily administered than our product candidates and may achieve patent protection or commercialize product candidates sooner than us. Any inability to compete successfully on our part will have a materially adverse impact on our business and operating results.

***If the market does not accept our technology and product candidates, we may not generate sufficient revenues to achieve or maintain profitability.***

The commercial success of our product candidates, even if approved for marketing by the FDA and corresponding foreign agencies, depends on their acceptance by the medical community and third-party payors as clinically useful, cost-effective and safe. Market acceptance, and thus sales of our products, will depend on several factors, including:

safety;

cost-effectiveness relative to alternative therapies, methods or products;

availability of third-party reimbursement;

ease of administration;

clinical efficacy; and

availability of competitive products.

If any of our product candidates, when and if commercialized, do not achieve market acceptance, we may not generate sufficient revenues to achieve or maintain profitability.

In addition, market acceptance of our imaging product candidate will also depend on our ability and that of our strategic partners to educate the medical community and third-party payors about the benefits of diagnostic imaging with Vasovist-enhanced magnetic resonance angiography compared to imaging with other

## **Table of Contents**

technologies. While we believe that contrast agents are currently used in an estimated 25% to 35% of all MRI exams, there are no MRI agents approved by the FDA for vascular imaging. Furthermore, clinical use of magnetic resonance angiography has been limited and use of magnetic resonance angiography for some vascular disease imaging has occurred mainly in research and academic centers. Vasovist represents a new approach to imaging the non-coronary vascular system, and market acceptance both of magnetic resonance angiography as an appropriate imaging technique for the non-coronary vascular system, and of Vasovist, is critical to our success.

***We may not be able to keep up with the rapid technological change in the biotechnology and pharmaceutical industries, which could make any of our future approved therapeutic products obsolete and reduce our revenue.***

Biotechnology and related pharmaceutical technologies have undergone and continue to be subject to rapid and significant change. Our future will depend in large part on our ability to maintain a competitive position with respect to these technologies. We believe that our proprietary therapeutic product discovery technology and approach enables structure-based discovery and optimization of certain GPCR and ion channel-targeted drug candidates. However, our competitors may render our technologies obsolete by advances in existing GPCR and ion channel-targeted drug discovery approaches or the development of new or different approaches. In addition, any future therapeutic products that we develop, including our clinical-stage therapeutic product candidates, PRX-08066, PRX-00023, PRX-03140 and PRX-07034, may become obsolete before we recover expenses incurred in developing those therapeutic product candidates, which may require us to raise additional funds to continue our operations.

***We are currently focusing our imaging development efforts primarily on Vasovist and will have limited prospects for successful imaging operations if it does not prove successful.***

Since the merger with Predix, we are focusing our imaging development efforts on our lead imaging product candidate, Vasovist. Accordingly, we have decided to cease work on our research projects related to the development of EP-2104R. We are no longer allocating resources to any imaging research or clinical programs other than the efforts required to continue to pursue FDA approval of Vasovist. Our efforts may not lead to commercially successful imaging products for a number of reasons, including the inability to be proven safe and effective in clinical trials, the lack of regulatory approvals or obtaining regulatory approvals that are narrower than we seek, inadequate financial resources to complete the development and commercialization of our imaging product candidates or their lack of acceptance in the marketplace.

***Our product candidates require significant biological testing, preclinical testing, manufacturing and pharmaceutical development expertise and investment. We rely primarily on external partners to complete these activities.***

We have limited in-house biological and preclinical testing capabilities. Therefore, we rely heavily on third-parties to perform in vitro potency, in vivo functional efficacy, animal toxicology and pharmacokinetics testing prior to advancing our product candidates into clinical trials. We also do not have internal expertise to formulate our therapeutic product candidates. In addition, we do not have, nor do we currently have plans to develop, full-scale manufacturing capability for any of our product candidates, including Vasovist. We currently rely on Aptuit, Inc. and Thermo Fisher Scientific Inc. for our therapeutic drug product manufacturing and testing, and on Aptuit, Inc. and Johnson Matthey Pharma Services for the manufacture and testing of our active therapeutic pharmaceutical ingredients. Although we believe that we could replace these suppliers on commercially reasonable terms, if any of these third-parties fail to fulfill their obligations to us or do not successfully complete the testing in a timely or acceptable manner, our therapeutic product development efforts could be negatively impacted and/or delayed. We rely on Covidien as the primary manufacturer of Vasovist for any future human clinical trials and commercial use. Together with Bayer Schering Pharma AG, Germany, we are considering alternative manufacturing arrangements for Vasovist for commercial use, including the transfer of manufacturing to Bayer Schering Pharma AG, Germany.

Covidien currently manufactures imaging agents for other technologies that will compete with Vasovist. In the event that Covidien

## **Table of Contents**

fails to fulfill its manufacturing responsibilities satisfactorily, Bayer Schering Pharma AG, Germany has the right to purchase Vasovist from a third-party or to manufacture the compound itself. However, either course of action could materially delay the manufacture and development of Vasovist. Bayer Schering Pharma AG, Germany may not be able to find an alternative manufacturer. In addition, Bayer Schering Pharma AG, Germany may not be able to manufacture Vasovist itself in a timely manner or in sufficient quantities. If we experience a delay in manufacturing of Vasovist or any of our product candidates, it could result in a delay in their clinical testing, approval or commercialization and have a material adverse effect on our business, financial condition and results of operations.

***If we are unable to attract and retain key management and other personnel, it would hurt our ability to compete.***

Our future business and operating results depend in significant part upon our ability to attract and retain qualified directors, senior management and key technical personnel. Michael G. Kauffman, M.D., Ph.D., Andrew C.G. Uprichard, M.D. and Kim Cobleigh Drapkin, CPA, our Chief Executive Officer, President and Chief Financial Officer, respectively, are expected to play key roles moving forward. There can be no assurance that we will be able to retain Dr. Kauffman, Dr. Uprichard, Ms. Drapkin or any of our other key management and scientific personnel. The loss of any of our key management and other personnel, or their failure to perform their current positions could have a material adverse effect on our business, financial condition and results of operations, and our ability to achieve our business objectives or to operate or compete in our industry may be seriously impaired. Competition for personnel is intense and we may not be successful in attracting or retaining such personnel. If we were to lose these employees to our competition, we could spend a significant amount of time and resources to replace them, which would impair our research and development or commercialization efforts.

***Our research and development efforts may not result in product candidates appropriate for testing in human clinical trials.***

We have historically spent significant resources on research and development and preclinical studies of product candidates. However, these efforts may not result in the development of product candidates appropriate for testing in human clinical trials. For example, our research may result in product candidates that are not expected to be effective in treating diseases or may reveal safety concerns with respect to product candidates. We may postpone or terminate research and development of a product candidate or a program at any time for any reason such as the safety or effectiveness of the potential product, allocation of resources or unavailability of qualified research and development personnel. The failure to generate high-quality research and development candidates would negatively impact our ability to advance product candidates into human clinical testing and ultimately, negatively impact our ability to market and sell products.

***If we fail to get adequate levels of reimbursement from third-party payors for our product candidates after they are approved in the United States and abroad, we may have difficulty commercializing our product candidates.***

We believe that reimbursement in the future will be subject to increased restrictions, both in the United States and in foreign markets. We believe that the overall escalating cost of medical products and services has led to, and will continue to lead to, increased pressures on the health care industry, both foreign and domestic, to reduce the cost of products and services, including products offered by us. These third-party payors are increasingly attempting to contain healthcare costs by demanding price discounts or rebates and limiting both coverage on which drugs they will pay for and the amounts that they will pay for new products. As a result, they may not cover or provide adequate payment for our products. We might need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future products to such payors' satisfaction. Such studies might require us to commit a significant amount of management time and financial and other resources. Our future products might not ultimately be considered cost-effective. There can be no assurance, in either the United States or foreign markets, that third-party reimbursement will be available or adequate, that current reimbursement amounts will not be decreased in the future



or that future legislation,

## **Table of Contents**

regulation, or reimbursement policies of third-party payors will not otherwise adversely affect the demand for our product candidates or our ability to sell our product candidates on a profitable basis. The unavailability or inadequacy of third-party payor coverage or reimbursement could have a material adverse effect on our business, financial condition and results of operations.

Failure by physicians, hospitals and other users of our product candidate to obtain sufficient reimbursement from third-party payors for the procedures in which our product candidate would be used or adverse changes in governmental and private third-party payors' policies toward reimbursement for such procedures may have a material adverse effect on our ability to market our product candidate and, consequently, it could have an adverse effect on our business, financial condition and results of operations. If we obtain the necessary foreign regulatory approvals, market acceptance of our product candidates in international markets would be dependent, in part, upon the availability of reimbursement within prevailing healthcare payment systems. Reimbursement and healthcare payment systems in international markets vary significantly by country, and include both government sponsored health care and private insurance. We and our strategic partners intend to seek international reimbursement approvals, although we cannot assure you that any such approvals will be obtained in a timely manner, if at all, and failure to receive international reimbursement approvals could have an adverse effect on market acceptance of our product candidate in the international markets in which such approvals are sought.

We could be adversely affected by changes in reimbursement policies of governmental or private healthcare payors, particularly to the extent any such changes affect reimbursement for procedures in which our product candidates would be used. U.S. and foreign governments continue to propose and pass legislation designed to reduce the cost of healthcare. For example, in some foreign markets, the government controls the pricing of prescription pharmaceuticals. In the United States, we expect that there will continue to be federal and state proposals to implement similar governmental controls. In addition, recent changes in the Medicare program and increasing emphasis on managed care in the United States will continue to put pressure on pharmaceutical product pricing. Cost control initiatives could decrease the price that we would receive for any products in the future, which would limit our revenue and profitability. Accordingly, legislation and regulations affecting the pricing of pharmaceuticals might change before our product candidates are approved for marketing. Adoption of such legislation could further limit reimbursement for pharmaceuticals.

***We deal with hazardous materials and must comply with environmental laws and regulations, which can be expensive and restrict how we do business.***

The nature of our research and development processes requires the use of hazardous substances and testing on certain laboratory animals. Accordingly, we are subject to extensive federal, state and local laws, rules, regulations and policies governing the use, generation, manufacture, storage, air emission, effluent discharge, handling and disposal of certain materials and wastes as well as the use of and care for laboratory animals. Although we are not currently, nor have we been, the subject of any investigations by a regulatory authority, we cannot assure you that we will not become the subject of any such investigation. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials.

In the event of an accident, state or federal authorities may curtail our use of these materials and interrupt our business operations. In addition, we could be liable for any civil damages that result, which may exceed our financial resources and may seriously harm our business. Due to the small amount of hazardous materials that we generate, we have determined that the cost to secure insurance coverage for environmental liability and toxic tort claims far exceeds the benefits. Accordingly, we do not maintain any insurance to cover pollution conditions or other extraordinary or unanticipated events relating to our use and disposal of hazardous materials. Additionally, an accident could damage, or force us to shut down, our operations. In addition, if we develop a manufacturing capacity, we may incur

substantial costs to comply with environmental regulations and would be subject to the risk of accidental contamination or injury from the use of hazardous materials in our manufacturing process. Furthermore, current laws could change and new laws could be passed that may force us to change our policies and procedures, an event which could impose significant costs on us.

**Table of Contents**

***Product liability claims could increase our costs and adversely affect our results of operations.***

The clinical testing of our products and the manufacturing and marketing of any approved products may expose us to product liability claims and we may experience material product liability losses in the future. We currently have limited product liability insurance for the use of our approved products and product candidates in clinical research, which is capped at \$10.0 million, but our coverage may not continue to be available on terms acceptable to us or adequate for liabilities we actually incur. We do not have product liability insurance coverage for the commercial sale of our product candidates, but intend to obtain such coverage when and if we commercialize our product candidates. However, we may not be able to obtain adequate additional product liability insurance coverage on acceptable terms, if at all. A successful claim brought against us in excess of available insurance coverage, or any claim or product recall that results in significant adverse publicity against us, may have a material adverse effect on our business and results of operations.

***Political and military instability and other factors may adversely affect our operations in Israel.***

We have significant operations in Israel and regional instability, military conditions, terrorist attacks, security concerns and other factors in Israel may directly affect these operations. Our employees in Israel are primarily computational chemists and are responsible for the computational chemistry for all of our therapeutic discovery stage programs. Accordingly, any disruption in our Israeli operations could adversely affect our ability to advance our therapeutic discovery stage programs into clinical trials. Since the establishment of the State of Israel in 1948, a number of armed conflicts have taken place between Israel and its Arab neighbors. A state of hostility, varying in degree and intensity, has led to security and economic problems for Israel, and in particular since 2000, there has been an increased level of violence between Israel and the Palestinians. Any armed conflicts or political instability in the region could harm our operations in Israel. In addition, many of our employees in Israel are obligated to perform annual military reserve duty, and, in the event of a war, military or other conflict, our employees could be required to serve in the military for extended periods of time. Our operations could be disrupted by the absence for a significant period of time of one or more of our key employees or a significant number of our other employees due to military service. Furthermore, several countries restrict business with Israel and Israeli companies, and these restrictive laws and policies could harm our business.

**RISKS RELATED TO OUR INTELLECTUAL PROPERTY**

***We depend on patents and other proprietary rights, and if they fail to protect our business, we may not be able to compete effectively.***

The protection of our proprietary technologies is material to our business prospects. We pursue patents for our product candidates in the United States and in other countries where we believe that significant market opportunities exist. We own or license patents and patent applications on aspects of our core technology as well as many specific applications of this technology. As of February 28, 2008, our patent portfolio included a total of 16 issued U.S. patents, 117 issued foreign patents, and 277 pending patent applications in the U.S. and other countries with claims covering the composition of matter and methods of use for all of our preclinical and clinical-stage product candidates. We also exclusively license technology embodied in patent applications from Ramot at Tel Aviv University Ltd., the technology transfer company of Tel Aviv University. Physiome Sciences, Inc., a predecessor of Predix, received U.S. Patent 5,947,899, which covers a computational system and method for modeling the heart. This patent expires in 2016. Even though we hold numerous patents and have made numerous patent applications, because the patent positions of pharmaceutical and biopharmaceutical firms, including our patent positions, generally include complex legal and factual questions, our patent positions remain uncertain. For example, because most patent applications are maintained in secrecy for a period after filing, we cannot be certain that the named applicants or inventors of the

subject matter covered by our patent applications or patents, whether directly owned or licensed to us, were the first to invent or the first to file patent applications for such inventions. Third-parties may oppose, challenge, infringe upon, circumvent or seek to invalidate existing or future patents owned by or licensed to us. A court or other agency with jurisdiction may find our patents invalid, not infringed or unenforceable and we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent

## **Table of Contents**

applications filed by us in the future. Even if we have valid patents, these patents still may not provide sufficient protection against competing products or processes. If we are unable to successfully protect our proprietary methods and technologies, or if our patent applications do not result in issued patents, we may not be able to prevent other companies from practicing our technology and, as a result, our competitive position may be harmed.

***We depend on exclusively licensed technology from Ramot at Tel Aviv University Ltd. and Massachusetts General Hospital and, if we lose either of these licenses, it is unlikely we could obtain such technology elsewhere, which would have a material adverse effect on our business.***

Our proprietary drug discovery technology and approach is in part embodied in technology that we license from Ramot at Tel Aviv University Ltd., the technology transfer company of Tel Aviv University. All of our current clinical-stage therapeutic drug candidates, PRX-00023, PRX-03140, PRX-08066 and PRX-07034, were, at least in part, identified, characterized or developed using the licensed technology. We are required to make various payments to Ramot, as and when rights to any such drug candidates are ever sublicensed or any such drug candidates are commercialized. Because we have an ongoing obligation to pay annual minimum royalties to Ramot and the license expires upon the expiration of such obligation, the license may not expire. The license may, however, be terminated upon a breach by us or our bankruptcy. In addition, under the terms of a license agreement that we have with MGH, we are the exclusive licensee to certain imaging technology, which relates to royalties we receive and to Vasovist. The license agreement imposes various commercialization, sublicensing, royalty and other obligations on us. The license agreement expires on a country-by-country basis when the patents covered by the license agreement expire. The majority of these patents expired in November 2006. One of these patents has been extended through Supplementary Protection Certificates for Primovist through May 2011 in certain European countries. The license agreement does not contain a renewal provision. If we fail to comply with our obligations under either of these license agreements, the respective license could convert from exclusive to nonexclusive, or terminate entirely. It is unlikely that we would be able to obtain the technology licensed under either of these agreements elsewhere. Any such event would also mean that, with respect to our MGH license, we would not receive royalties from Bayer Schering Pharma AG, Germany for Primovist and that we or Bayer Schering Pharma AG, Germany could not sell Vasovist and, with respect to our Ramot license, that we would not be able to sublicense or commercialize any of our current clinical-stage therapeutic drug candidate, either of which would have a material adverse effect on our business and our financial condition and results of operations.

***We may need to initiate lawsuits to protect or enforce our patents and other intellectual property rights, which could result in our incurrence of substantial costs and which could result in the forfeiture of these rights.***

We may need to bring costly and time-consuming litigation against third-parties in order to enforce our issued or licensed patents, protect our trade secrets and know how, or to determine the enforceability, scope and validity of proprietary rights of others. In addition to being costly and time-consuming, such lawsuits could divert management's attention from other business concerns. These lawsuits could also result in the invalidation or a limitation in the scope of our patents or forfeiture of the rights associated with our patents or pending patent applications. We may not prevail and a court may find damages or award other remedies in favor of an opposing party in any such lawsuits. During the course of these suits, there may be public announcements of the results of hearings, motions and other interim proceedings or developments in the litigation. Securities analysts or investors may perceive these announcements to be negative, which could cause the market price of our stock to decline. In addition, the cost of such litigation could have a material adverse effect on our business and financial condition.

***Other rights and measures that we rely upon to protect our intellectual property may not be adequate to protect our products and services and could reduce our ability to compete in the market.***

In addition to patents, we rely on a combination of trade secrets, copyright and trademark laws, non-disclosure agreements and other contractual provisions and technical measures to protect our intellectual

## **Table of Contents**

property rights. While we require employees, collaborators, consultants and other third-parties to enter into confidentiality and/or non-disclosure agreements, where appropriate, any of the following could still occur:

the agreements may be breached;

we may have inadequate remedies for any breach;

proprietary information could be disclosed to our competitors; or

others may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose such technologies.

If, as a result of the foregoing or otherwise, our intellectual property is disclosed or misappropriated, it would harm our ability to protect our rights and our competitive position. Moreover, several of our management and scientific personnel were formerly associated with other pharmaceutical and biotechnology companies and academic institutions. In some cases, these individuals are conducting research in similar areas with which they were involved prior to joining us. As a result, we, as well as these individuals, could be subject to claims of violation of trade secrets and similar claims.

***Our success will depend partly on our ability to operate without infringing the intellectual property rights of others, and if we are unable to do so, we may not be able to sell our products.***

Our commercial success will depend, to a significant degree, on our ability to operate without infringing upon the patents of others in the United States and abroad. There may be pending or issued patents held by parties not affiliated with us relating to technologies we use in the development or use of certain of our contrast agents. If any judicial or administrative proceeding upholds these or any third-party patents as valid and enforceable, we could be prevented from practicing the subject matter claimed in such patents, or would be required to obtain licenses from the owners of each such patent, or to redesign our product candidates or processes to avoid infringement. For example, in November 2003, we entered into an intellectual property agreement with Dr. Martin R. Prince relating to dynamic magnetic resonance angiography. Under the terms of the intellectual property agreement, Dr. Prince granted us certain discharges, licenses and releases in connection with the historic and future use of Vasovist by us and agreed not to sue us for intellectual property infringement related to the use of Vasovist. We were required to pay an upfront fee of \$850,000, royalties on sales of Vasovist and approximately 88,000 shares of our common stock with a value of approximately \$2.3 million based on the closing price of our common stock on the date of the agreement. In addition, we agreed to supply Dr. Prince with approximately \$140,000 worth of Vasovist annually throughout the patent life of Vasovist. We cannot assure you that we will be able to enter into additional licenses if required in the future. If we are unable to obtain a required license on acceptable terms, or are unable to design around these or any third-party patents, we may be unable to sell our products, which would have a material adverse effect on our business.

***If MRI manufacturers are not able to enhance their hardware and software sufficiently, we will not be able to complete development of our contrast agent for the evaluation of cardiac indications.***

Although MRI hardware and software is sufficient for the evaluation of non-coronary vascular disease, which is our initial target indication, we believe that the technology is not as advanced for cardiac applications. Our initial NDA filing for Vasovist is related to non-coronary vascular disease. Based on feasibility studies we completed in 2001, however, the imaging technology available for cardiac applications, including coronary angiography and cardiac perfusion imaging, was not developed to the point where there was clear visualization of the cardiac region due to the effects of motion from breathing and from the beating of the heart. In 2004, we initiated Phase 2 feasibility trials of Vasovist for cardiac indications using available software and hardware that can be adapted for coronary and cardiac



perfusion data acquisition, and preliminary review of the data indicates that we have not resolved the technical issues related to this use of Vasovist. We have collaborated with a number of leading academic institutions and with GE Healthcare, Siemens Medical Systems and Philips Medical Systems to help optimize cardiac imaging with Vasovist. We do not know when, or if, these techniques will enable Vasovist to provide clinically relevant images in cardiac indications. If MRI device

## **Table of Contents**

manufacturers are not able to enhance their scanners to perform clinically useful cardiac imaging, we will not be able to complete our development activities of Vasovist for that application, thereby reducing the potential market for a product in this area.

## **RISKS RELATED TO OUR SECURITIES**

### ***Our stock price is volatile, which could subject us to securities class action litigation.***

The market prices of the capital stock of medical technology companies have historically been very volatile and the market price of the shares of our common stock fluctuates. The market price of our common stock is affected by numerous factors, including:

- actual or anticipated fluctuations in our operating results;
- announcements of technological innovation or new commercial products by us or our competitors;
- new collaborations entered into by us or our competitors;
- developments with respect to proprietary rights, including patent and litigation matters;
- results of preclinical studies and clinical trials;
- the timing of our achievement of regulatory milestones;
- conditions and trends in the pharmaceutical and other technology industries;
- adoption of new accounting standards affecting such industries;
- changes in financial estimates by securities analysts;
- perceptions of the value of corporate transactions; and
- degree of trading liquidity in our common stock and general market conditions.

From the closing of our merger with Predix and our 1 for 1.5 share reverse stock split on August 16, 2006 to March 14, 2008, the closing price of our common stock ranged from \$2.67 to \$7.58 per share. The last reported closing price for our common stock on March 14, 2008 was \$2.85. Significant declines in the price of our common stock could impede our ability to obtain additional capital, attract and retain qualified employees and reduce the liquidity of our common stock.

In addition, the stock market has from time to time experienced significant price and volume fluctuations that have particularly affected the market prices for the common stock of similarly staged companies. These broad market fluctuations may adversely affect the market price of our common stock. In the past, following periods of volatility in the market price of a particular company's securities, shareholders have often brought class action securities litigation against that company. Such litigation could result in substantial costs and a diversion of management's attention and resources. For example, in January 2005, a securities class action was filed in U.S. District Court for the District of Massachusetts against us and certain of our officers on behalf of persons who purchased our common stock between July 10, 2003 and January 14, 2005. The complaint alleged that we and the other defendants violated the Securities Exchange Act of 1934, as amended, by issuing a series of materially false and misleading statements to the market

throughout the class period, which statements had the effect of artificially inflating the market price of our securities. In January 2006, the U.S. District Court for the District of Massachusetts granted our Motion to Dismiss for Failure to Prosecute the shareholder class action lawsuit against us. The dismissal was issued without prejudice after a hearing, which dismissal does not prevent another suit to be brought based on the same claims.

***Future sales of common stock by our existing stockholders and former security holders of Predix may cause the stock price of our common stock to fall.***

The market price of our common stock could decline as a result of sales by our existing stockholders and former Predix stockholders in the market, or the perception that these sales could occur. These sales might also make it more difficult for us to sell equity securities at an appropriate time and price.

**Table of Contents**

***Certain anti-takeover clauses in our charter and by-laws and in Delaware law may make an acquisition of us more difficult.***

Our restated certificate of incorporation authorizes our board of directors to issue, without stockholder approval, up to 1,000,000 shares of preferred stock with voting, conversion and other rights and preferences that could adversely affect the voting power or other rights of the holders of our common stock. The issuance of preferred stock or of rights to purchase preferred stock could be used to discourage an unsolicited acquisition proposal. In addition, the possible issuance of preferred stock could discourage a proxy contest, make more difficult the acquisition of a substantial block of our common stock or limit the price that investors might be willing to pay for shares of our common stock. Our restated certificate of incorporation provides for staggered terms for the members of our board of directors. A staggered board of directors and certain provisions of our by-laws and of the state of Delaware law applicable to us could delay or make more difficult a merger, tender offer or proxy contest involving us. We are subject to Section 203 of the General Corporation Law of the State of Delaware, which, subject to certain exceptions, restricts certain transactions and business combinations between a corporation and a stockholder owning 15% or more of the corporation's outstanding voting stock for a period of three years from the date the stockholder becomes an interested stockholder. These provisions may have the effect of delaying or preventing a change in control of us without action by the stockholders and, therefore, could adversely affect the price of our stock.

**RISKS RELATING TO OUR PRIVATE PLACEMENT**

***If we do not maintain effectiveness of the registration statements covering the resale of the shares issued in the November 2007 private placement, we will be required to pay certain liquidated damages, which could be material in amount.***

The terms of the securities purchase agreements in connection with the private placement would require us to pay certain liquidated damages to the purchasers in the private placement in the event that the registration statement does not remain effective until the earlier of (i) 3 years after the closing, (ii) the date on which all shares purchased by such purchasers may be sold under Rule 144(k) of the Securities Act of 1933, as amended, or (iii) the date that all of the shares have been sold by such purchasers. The only exception is our right, without incurring liquidated damages, to suspend the use of the registration statement during three periods of no more than an aggregate of 60 days in any 12-month period. Subject to this exception, for each 30-day period when the registration statement is not effective, we are obligated to pay to each purchaser an amount in cash equal to 1% of that purchaser's aggregate purchase price, up to a maximum of 10% of the aggregate purchase price paid by that purchaser. The foregoing payments apply on a pro rata basis for any portion of such 30-day period. These amounts could be material. If we are unable to maintain the effectiveness of the registration statement (or effectiveness is suspended other than as provided in the securities purchase agreements), the amounts we are required to pay could materially adversely affect our financial condition.

**SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS**

This prospectus and the documents incorporated herein by reference contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements relate to future events or to our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance, or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. These statements are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities and Exchange Act of 1934, as amended, and are intended to be covered by the safe harbor created by those sections. Forward-looking statements, which are based on certain assumptions and reflect our plans, estimates and beliefs, can generally be identified by the use of forward-looking terms such as

believes, expects, may, will, should, could, seek, intends, plans, estimates, anticipates or other actual results could differ materially from those discussed in the forward-looking statements. We caution

## **Table of Contents**

readers not to place undue reliance upon any such forward-looking statements, which speak only as of the date made. Factors that may cause actual results to differ materially from current expectations, which we describe in more detail elsewhere in this prospectus under the heading "Risk Factors," include, but are not limited to:

the competitive environment in the life sciences industry;

whether we can successfully develop new products and the degree to which these gain market acceptance;

the success and timing of our pre-clinical studies and clinical trials;

our ability to obtain and maintain regulatory approval for our product candidates and the timing of such approvals;

our ability to research, develop and commercialize our product candidates;

regulatory developments in the United States and foreign countries; and

our ability to obtain and maintain intellectual property protection for our product candidates.

If one or more of these or other risks or uncertainties materialize, or if our underlying assumptions prove to be incorrect, actual results may vary significantly from what we projected. Any forward-looking statement you read in this prospectus reflects our current views with respect to future events and is subject to these and other risks, uncertainties and assumptions relating to our operations, results of operations, growth strategy and liquidity. We assume no obligation to publicly update or revise these forward-looking statements for any reason, or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

The safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995 protects companies from liability for their forward looking statements if they comply with the requirements of the Act.

## **USE OF PROCEEDS**

We will not receive any proceeds from the sale or other disposition by the selling stockholders of the shares of our common stock covered hereby, or interests therein. The selling stockholders will pay any underwriting discounts and commissions and expenses incurred by the selling stockholders for brokerage, accounting, tax or legal services or any other expenses incurred by the selling stockholders in disposing of these shares. We will bear all other costs, fees and expenses incurred in effecting the registration of the shares covered by this prospectus, including, without limitation, all registration and filing fees, NASDAQ Global Market listing fees and fees and expenses of our counsel and our accountants.

## **SELLING STOCKHOLDERS**

The shares of common stock covered hereby consist of 5,245,468 shares of our common stock that we issued to the selling stockholders in the private placement that closed on November 15, 2007.

In connection with the registration rights we granted to the selling stockholders, we agreed to file with the Securities and Exchange Commission, or SEC, a registration statement on Form S-1, of which this prospectus forms a part, with respect to the resale or other disposition of the shares of common stock offered by this prospectus or interests therein from time to time on the NASDAQ Global Market, in privately negotiated transactions or otherwise. We have also

agreed to prepare and file amendments and supplements to the registration statement to the extent necessary to keep the registration statement effective for the period of time required under our agreement with the selling stockholders.

Beneficial ownership is determined in accordance with the rules of the SEC, and is based upon information provided by each respective selling stockholder. The number representing the number of shares of common stock beneficially owned prior to the offering for each selling stockholder includes (i) all shares held by a selling stockholder prior to the private placement, plus (ii) all shares purchased by the selling stockholder

**Table of Contents**

in the private placement and being offered pursuant to the prospectus, as well as (iii) all options or other derivative securities which are exercisable within 60 days of November 16, 2007. The percentages of shares owned are based on 41,311,679 shares of our common stock outstanding as of November 16, 2007, which includes the outstanding shares of common stock offered by this prospectus.

Unless otherwise indicated below, to our knowledge, all persons named in this table have sole voting and investment power with respect to their shares of common stock, except to the extent authority is shared by spouses under applicable law. The inclusion of any shares in this table does not constitute an admission of beneficial ownership for the person named below.

None of the selling stockholders has held any position or office with us or our affiliates within the last three years or has had a material relationship with us or any of our predecessors or affiliates within the past three years, other than as a result of the ownership of our shares or other securities.

The selling stockholders may sell some, all or none of their shares of common stock offered by this prospectus. We do not know how long the selling stockholders will hold their shares of common stock before selling them. We currently have no agreements, arrangements or understandings with the selling stockholders regarding the sale of any of the shares of common stock being offered hereunder other than the securities purchase agreement pursuant to which the selling stockholders purchased their shares of common stock from us. The shares offered by this prospectus may be offered from time to time by the selling stockholders. Accordingly, for purposes of this table, we have assumed that, after completion of the offering, the only shares that will continue to be held by the selling stockholders are those that were owned immediately prior to the private placement.

The selling stockholders may have sold or transferred, in transactions exempt from the registration requirements of the Securities Act of 1933, as amended, or the Securities Act, some or all of their shares of common stock since the date on which the information in the table below is presented. Information about the selling stockholders may change over time.



**Table of Contents**

The following table sets forth, to our knowledge, information about the selling stockholders as of November 16, 2007, except as otherwise referenced below.

| Name of Selling Stockholder(1)   | Shares of Common<br>Stock Beneficially<br>Owned Prior<br>to the Offering |         | Shares of<br>Common<br>Stock<br>Registered<br>for Sale<br>Hereby | Shares of<br>Common Stock<br>Beneficially Owned After<br>the Completion of the<br>Offering |         |
|--|--|---------|--|--|---------|
|  | Number   | Percent |  | Number   | Percent |
| Diamond Opportunity Fund, LLC(2)   | 161,290  | *       | 161,290  |  |         |
| Henry C. Beinstein(3)  | 323,686  | *       | 96,774   | 226,912  | *       |
| Prescott Group Aggressive Small Cap<br>Master Fund, G.P.(4)                      | 2,734,675  | 6.62%   | 806,452  | 1,928,223  | 4.67%   |
| SF Capital Partners Ltd.(5)  | 1,612,903  | 3.90%   | 1,612,903  |  |         |
| SRB Greenway Capital Entities(6)   | 322,581  | *       | 322,581  |  |         |
| Steelhead Investments Ltd.(7)  | 483,871  | 1.17%   | 483,871  |  |         |
| T. Rowe Price Health Sciences Fund,<br>Inc.(8)                                   | 500,000  | 1.21%   | 100,000  | 400,000  | *       |
| T. Rowe Price Health Sciences<br>Portfolio, Inc.(8)                              | 4,700  | *       | 1,200  | 3,500  | *       |
| TD Mutual Funds TD Health Sciences<br>Fund(8)                                    | 47,400   | *       | 9,100  | 38,300   | *       |
| Valic Company I Health Sciences<br>Fund(8)                                       | 46,600   | *       | 14,100   | 32,500   | *       |
| John Hancock Trust Health Sciences<br>Trust(8)                                   | 58,400   | *       | 16,600   | 41,800   | *       |
| Raytheon Company Combined DB/DC<br>Master Trust Health Sciences(8)               | 7,100  | *       | 2,700  | 4,400  | *       |
| T. Rowe Price New Horizons Fund,<br>Inc.(8)                                      | 2,550,000  | 6.17%   | 226,365  | 2,323,635  | 5.63%   |
| City of New York Deferred<br>Compensation Plan NYC 457/401K<br>Small Cap(8)      | 69,800   | *       | 6,400  | 63,400   | *       |
| T. Rowe Price New Horizons Trust(8)  | 74,000   | *       | 6,100  | 67,900   | *       |
| UBS O Connor LLC FBO O Connor<br>PIPES Corporate Strategies Master<br>Limited(9) | 250,000  | *       | 250,000  |  |         |
| Walker Smith Entities(10)  | 161,290  | *       | 161,290  |  |         |
| Westfield Capital Management<br>Entities(11)                                     | 1,505,990  | 3.65%   | 967,742  | 538,248  | 1.30%   |

\* less than 1%

- (1) Throughout this prospectus, when we refer to the selling stockholders, we mean the persons listed in the table above, as well as the pledges, donees, assignees, transferees, successors and others who later hold any of the selling stockholders' interests, and when we refer to the shares of our common stock being offered by this prospectus on behalf of the selling stockholders, we are referring to the shares of our common stock sold in the private placement, collectively, unless otherwise indicated.
- (2) Diamond Asset Management, LLC is the manager of Diamond Opportunity Fund, LLC and, in such capacity, exercises sole voting and investment power with respect to such shares held by Diamond Opportunity Fund, LLC. David Hokin, Rub Rubin and Richard Marks serve as the Managers and Managing Director, respectively, of Diamond Asset Management, LLC and may be deemed to have shared voting and investment power with respect to such shares. Diamond Asset Management, LLC and each of Messrs. Hokin, Rubin and Marks disclaim beneficial ownership of such shares and disclaim beneficial ownership of the shares except to the extent of its or his pecuniary interest. The principal address for Diamond Opportunity Fund, LLC is 500 Skokie Boulevard, Suite 300, Northbrook, IL 60062.
- (3) Includes 226,912 shares held by Gagnon Securities LLC. As a partner of Gagnon Securities LLC, Henry C. Beinstein may be deemed to share voting and investment power with respect to the shares held

**Table of Contents**

by Gagnon Securities LLC. Mr. Beinstein disclaims beneficial ownership of the shares held by Gagnon Securities LLC except to the extent of his pecuniary interest, if any. The principal address for Mr. Beinstein is 8 Dogwood Lane, Larchmont, NY 10538.

- (4) Phil Frolich is the manager of Prescott Group Aggressive Small Cap Master Fund, G.P. and has voting and investment power with respect to such shares. Mr. Frolich disclaims beneficial ownership of such shares except to the extent of his pecuniary interest, if any. The principal address for Prescott Group Aggressive Small Cap Master Fund, G.P. is 1924 South Utica, Suite 1120, Tulsa, OK 74104.
- (5) Michael A. Roth and Brian J. Stark each have voting and investment power with respect to such shares. Messrs. Roth and Stark each disclaim beneficial ownership of such shares except to the extent of his pecuniary interest, if any. The principal address for SF Capital Partners Ltd. is c/o Stark Offshore Management Ltd., 3600 South Lake Drive, St. Francis, WI 53235.
- (6) Consists of 32,097 shares held by SRB Greenway Capital, L.P., 278,484 shares held by SRB Greenway Capital (QP), L.P., and 12,000 shares held by SRB Greenway Offshore Operating Fund, L.P. SRB Management, L.P. is the General Partner of each of these entities, and BC Advisors, LLC is the General Partner of SRB Management L.P. As Managing Member of BC Advisors, LLC, Steven R. Becker has voting and investment power with respect to all shares held by these entities. BC Advisors, LLC, SRB Management L.P. and Mr. Becker each disclaim beneficial ownership of these shares except to the extent of its or his pecuniary interest, if any. The principal address for each of SRB Greenway Capital, L.P., SRB Greenway Capital (QP), L.P. and SRB Greenway Offshore Operating Fund, L.P. is 300 Crescent Court, Suite 1111, Dallas, TX 75201.
- (7) HBK Investments L.P., a Delaware limited partnership, has shared voting and investment power over the shares pursuant to an Investment Management Agreement between HBK Investments L.P. and Steelhead Investments Ltd. HBK Investments L.P. has delegated voting and investment power to HBK Services LLC. Jamiel A. Akhtar, Richard L. Booth, David C. Haley, Laurence H. Lebowitz and William E. Rose are each a Managing Director of HBK Investments L.P. and each may be deemed to have voting and investment power with respect to such shares. Each of these individuals disclaims beneficial ownership of the shares except to the extent of his pecuniary interest, if any. The principal address for Steelhead Investments Ltd. is c/o HBK Services LLC, 300 Crescent Court, Suite 700, Dallas, TX 75201.
- (8) T. Rowe Price Associates, Inc., or TRPA, serves as investment advisor to this entity and has voting and investment power with respect to all shares held by this entity. TRPA disclaims beneficial ownership of the shares except to the extent of its pecuniary interest, if any. TRPA is the wholly-owned subsidiary of T. Rowe Price Group, Inc., which is a publicly traded financial services holding company. The principal address for TRPA is 100 East Pratt Street, Baltimore, MD 21202. The beneficial holdings listed is as of November 8, 2007.
- (9) UBS O Connor LLC, as investment manager, has voting and investment power with respect to the shares held by UBS O Connor LLC FBO O Connor PIPES Corporate Strategies Master Limited. UBS O Connor LLC disclaims beneficial ownership of such shares except to the extent of its pecuniary interest, if any. UBS O Connor LLC is a wholly-owned subsidiary of UBS AG, which is listed and traded on the New York Stock Exchange. The principal address for UBS O Connor LLC FBO O Connor PIPES Corporate Strategies Master Limited is c/o UBS O Connor LLC, One North Wacker Drive, 3<sup>rd</sup> Floor, Chicago, IL 60606.
- (10) Consists of 46,129 shares held by WS Opportunity Fund, L.P. ( WSO ), 43,484 shares held by WS Opportunity Fund (QP), L.P. ( WSOQP ), and 71,677 shares held by WS Opportunity Fund International, Ltd ( WSOFI ). WS Ventures Management, L.P. ( WSVM ) is the General Partner of WSO and WSOQP and the agent and attorney-in-fact of WSOFI. WSV Management, LLC ( WSV ) is the General Partner of WSVM. Reid S. Walker,

G. Stacy Smith and Patrick P. Walker are the Sole Members of WSV, and each have voting and investment power with respect to all shares held by these entities. Each of WSV, WSVM, Messrs. Walker, Walker and Smith disclaims beneficial ownership of such shares except to the extent of its or his pecuniary interest, if any. The principal address for each of WSO, WSOQP and WSOFI is 300 Crescent Court, Suite 1111, Dallas, TX 75201.

**Table of Contents**

- (11) Consists of 113,677 shares held by Westfield Life Sciences Fund LP ( WLSF ) and 1,392,313 shares held by Westfield Life Sciences Fund II LP ( WLSFII ). Westfield Capital Management Company ( WCMC ) is the investment advisor to each of WLSF and WLSFII, and William Albert Muggia, as General Partner of each of WLSF and WLSFII, has voting and investment power with respect to all shares held by these entities. WCMC and Mr. Muggia each disclaim beneficial ownership of such shares except to the extent of its or his pecuniary interest, if any. The principal address for each of WLSF and WLSFII is c/o Westfield Capital Management Company, One Financial Center, 24<sup>th</sup> Floor, Boston, MA 02111.

**REGISTRATION RIGHTS**

The following is a summary of material terms and provisions of the securities purchase agreements which we entered into with the selling stockholders. It may not contain all the information that is important to you. You can access complete information by referring to the form of securities purchase agreement.

Under the securities purchase agreements, we have agreed, subject to receipt of necessary information from the purchasers, to use our reasonable best efforts to cause a registration statement covering the resale of the shares purchased by the selling stockholders to be filed with the SEC no later than 30 days after the closing date of the purchase.

Subject to certain exempt periods set forth in the securities purchase agreements, we are obligated to use our commercially reasonable efforts, with respect to each selling stockholder's shares, to maintain the registration statement's effectiveness until the earlier of (i) three years from the closing date of the purchase; (ii) the date on which all shares purchased by such selling stockholder may be sold under Rule 144(k) of the Securities Act; or (iii) the date that all of the shares have been sold by such selling stockholder. In the event that the registration statement is not filed by us or declared effective by the SEC within the specified time period, or the effectiveness of such registration statement is suspended for certain periods, which we refer to as a Registration Default, we shall pay each selling stockholder, for each 30-day period of a Registration Default, an amount in cash equal to 1% of the aggregate purchase price paid by the selling stockholder; provided that in no event shall the aggregate amount of cash to be paid exceed 10% of the aggregate purchase price. The foregoing payments shall apply on a pro rata basis for any portion of a 30-day period of a Registration Default.

In addition, we will pay all costs, expenses and fees in connection with the registration of the shares of common stock, including, without limitation, all registration, qualification and filing fees, printing expenses, escrow fees, fees and expenses of our counsel, blue sky fees and expenses and the expense of any special audits incident to or required by the registration. The selling stockholders will be responsible for all expenses relating to the sale of the shares of common stock, including selling commissions and stock transfer taxes applicable to the sale of the shares of common stock and all fees and expenses of legal counsel for the selling stockholders. The securities purchase agreements also contain mutual indemnification provisions among the parties.

**PLAN OF DISTRIBUTION**

The selling stockholders, and any of their pledgees, assignees and successors-in-interest (including successors by gift, partnership distribution or other non-sale-related transfer effected after the date of this prospectus), may, from time to time, sell any or all of their shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These sales may be at fixed prices, at market prices at the time of sale, at varying prices determined at the time of sale or at negotiated prices. The selling stockholders may use any one or more of the following methods when selling shares:

ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;

block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;

purchases by a broker-dealer as principal and resale by the broker-dealer for its account;

an exchange distribution in accordance with the rules of the applicable exchange;

privately negotiated transactions;

**Table of Contents**

short sales;

broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;

a combination of any such methods of sale; and

any other method permitted pursuant to applicable law.

The selling stockholders may also sell shares under Rule 144 under the Securities Act of 1933, as amended, or the Securities Act, if available, rather than under this prospectus. The selling stockholders are not obligated to, and there is no assurance that the selling stockholders will, sell all or any of the shares we are registering. The selling stockholders may transfer, devise or gift such shares by other means not described in this prospectus.

The selling stockholders may also engage in short sales against the box, puts and calls and other transactions in our securities or derivatives of our securities and may sell or deliver shares in connection with these trades.

Broker-dealers engaged by the selling stockholders may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling stockholders (or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated. The selling stockholders do not expect these commissions and discounts to exceed what is customary in the types of transactions involved. Any profits on the resale of shares of common stock by a broker-dealer acting as principal might be deemed to be underwriting discounts or commissions under the Securities Act. Discounts, concessions, commissions and similar selling expenses, if any, attributable to the sale of shares will be borne by a selling stockholder. The selling stockholders may agree to indemnify any agent, dealer or broker-dealer that participates in transactions involving sales of the shares if liabilities are imposed on that person under the Securities Act. The selling stockholders that are also broker-dealers are underwriters within the meaning of the Securities Act.

The selling stockholders may from time to time pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of any of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock from time to time under this prospectus as it may be supplemented from time to time, or under an amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus.

The selling stockholders also may transfer the shares of common stock in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

The selling stockholders have advised us that they have not entered into any agreements, understandings or arrangements with any underwriters or broker-dealers regarding the sale of their shares of common stock, nor is there an underwriter or coordinating broker acting in connection with a proposed sale of shares of common stock by any selling stockholder. If we are notified by any selling stockholder that any material arrangement has been entered into with a broker-dealer for the sale of shares of common stock, if required, we will file a supplement to this prospectus. If the selling stockholders use this prospectus for any sale of the shares of common stock, they will be subject to the prospectus delivery requirements of the Securities Act.

The anti-manipulation rules of Regulation M under the Securities Exchange Act of 1934 may apply to sales of our common stock and activities of the selling stockholders. We will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling stockholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling stockholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.



**Table of Contents**

**LEGAL MATTERS**

Goodwin Procter llp, Boston, Massachusetts, has passed upon the validity of the shares of common stock offered hereby.

**EXPERTS**

The consolidated financial statements of EPIX Pharmaceuticals, Inc. appearing in EPIX Pharmaceuticals, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2007, and the effectiveness of EPIX Pharmaceuticals, Inc. internal control over financial reporting as of December 31, 2007 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such reports given on the authority of such firm as experts in accounting and auditing.

**WHERE YOU CAN FIND MORE INFORMATION**

We have filed with the SEC a registration statement on Form S-1 under the Securities Act of 1933 with respect to the shares of common stock we are offering by this prospectus. This prospectus does not contain all of the information included in the registration statement. For further information pertaining to us and our common stock, you should refer to the registration statement and to its exhibits. Whenever we make reference in this prospectus to any of our contracts, agreements or other documents, the references are not necessarily complete, and you should refer to the exhibits attached to the registration statement for copies of the actual contract, agreement or other document.

We are subject to the informational requirements of the Securities Exchange Act of 1934 and file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, over the Internet at the SEC's website at [www.sec.gov](http://www.sec.gov). You may also read and copy any document we file with the SEC at its public reference facility at 100 F Street, N.E., Washington, D.C., 20549.

You may also obtain copies of the documents at prescribed rates by writing to the Public Reference Section of the SEC at 100 F Street, N.E., Washington, D.C., 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference facility.

**INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE**

The SEC allows us to incorporate by reference certain of our publicly-filed documents into this prospectus, which means that information included in those documents is considered part of this prospectus.

The following documents filed with the SEC are incorporated by reference into this prospectus:

our Annual Report on Form 10-K for the year ended December 31, 2007;

those portions of our Proxy Statement filed with the SEC on April 30, 2007 incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2006;

our Current Report on Form 8-K filed with the SEC on February 22, 2008; and

the description of our common stock contained in Description of Capital Stock in the registration statement on Form S-4 filed with the SEC on April 25, 2006 (File No. 333-133513) and any amendments or reports filed to update such description.

You may access our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to any of these reports, free of charge on the SEC's website. We do not consider information contained on, or that can be accessed through, our website to be part of this prospectus.

**Table of Contents**

In addition, we will furnish without charge to you, on written or oral request, a copy of any or all of the documents incorporated by reference, other than exhibits to those documents. You should direct any requests for documents to Chief Financial Officer, EPIX Pharmaceuticals, Inc., 4 Maguire Road, Lexington, Massachusetts 02421, or call (781) 761-7600.

You should rely only on the information contained in this prospectus, including information incorporated by reference herein. We have not authorized anyone to provide you with information different from that contained in this prospectus or any prospectus supplement. This prospectus is not an offer of these securities in any jurisdiction where an offer and sale is not permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sale of our common stock.

**Table of Contents****Part II****INFORMATION NOT REQUIRED IN PROSPECTUS****Item 13. *Other expenses of issuance and distribution.***

The following table sets forth the costs and expenses, other than the underwriting discount, payable by us in connection with the sale of common stock being registered. All amounts are estimated except the SEC registration fee.

|                                  | <b>Amount to be Paid</b> |
|----------------------------------|--------------------------|
| SEC registration fee             | \$ 485                   |
| NASDAQ Global Market listing fee | \$ 65,000                |
| Printing expenses                | \$ 10,000                |
| Legal fees and expenses          | \$ 100,000               |
| Accounting fees and expenses     | \$ 20,000                |
| Transfer agent and registrar     | \$ 2,500                 |
| <br>Total                        | <br>\$ 197,985           |

**Item 14. *Indemnification of directors and officers.***

Our Restated Certificate of Incorporation, as amended (the "Restated Certificate") provides that we shall indemnify to the fullest extent authorized by the Delaware General Corporation Law ( "DGCL"), each person who is involved in any litigation or other proceeding because such person is or was a director or officer of us or is or was serving as an officer or director of another entity at our request, against expenses (including attorney's fees), judgments, fines and amounts reasonably incurred in connection therewith. The Restated Certificate provides that the right to indemnification includes the right to be paid expenses incurred in defending any proceeding in advance of its final disposition; provided, however, that such advance payment will only be made upon delivery to us of an undertaking, by the director or officer, to repay all amounts so advanced if it is ultimately determined that such director or officer is not entitled to indemnification.

Section 145 of the DGCL permits a corporation to indemnify any director or officer of the corporation against expenses (including attorney's fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with any action, suit or proceeding brought by reason of the fact that such person is or was a director or officer of the corporation, if such person acted in good faith and in a manner that he or she reasonably believed to be in, or not opposed to, the best interests of the corporation, and, with respect to any criminal action or proceeding, if he or she had no reason to believe his or her conduct was unlawful. In a derivative action, (i.e., one brought by or on behalf of the corporation), indemnification may be made only for expenses, actually and reasonably incurred by any director or officer in connection with the defense or settlement of such an action or suit, if such person acted in good faith and in a manner that he reasonably believed to be in, or not opposed to, the best interests of the corporation, except that no indemnification shall be made if such person shall have been adjudged to be liable to the corporation, unless and only to the extent that the court in which the action or suit was brought shall determine that the defendant is fairly and reasonably entitled to indemnity for such expenses despite such adjudication of liability.

Pursuant to Section 102(b)(7) of the DGCL, the Restated Certificate eliminates the liability of a director or the corporation or its stockholders for monetary damages for such breach of fiduciary duty as a director, except for liabilities arising (i) from any breach of the director's duty of loyalty to the corporation or its stockholders, (ii) from

acts or missions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under Section 174 of the DGCL, or (iv) from any transaction from which the director derived an improper personal benefit. We have obtained insurance policies insuring our directors and officers against certain liabilities that they may incur in their capacity as directors and officers.

II-1

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**Table of Contents**

We have entered, or intend to enter, into indemnification agreements (the Indemnification Agreements ), with each of our directors and certain of our officers. The Indemnification Agreements provide that we will, to the fullest extent permitted by law, pay any attorneys fees and all other costs, expenses and obligations paid or incurred by the indemnitee in connection with claims against him or her related to the fact that he or she was a director or officer of the company or serving at our request in such capacity with another corporation, partnership, joint venture, employee benefit plan, trust or other enterprise. The payments to be made under the Indemnification Agreements include expenses, judgments, fines, penalties and amounts paid in settlement (including all interest, assessments and other judgments, fines, penalties or amounts paid in settlement) of such claims. If requested by the indemnitee, we shall advance all expenses to the indemnitee. Any payments made by us under the Indemnification Agreements are subrogated to all of the rights of recovery of the indemnitee. The rights of the indemnitee are in addition to such rights the indemnitee may have under our Restated Certificate, our by-laws and the DGCL.

Pursuant to the Agreement and Plan of Merger by and among us, Predix Pharmaceuticals Holdings, Inc. ( Predix ) and EPIX Delaware, Inc. dated as of April 3, 2006, as amended, we agreed to fulfill and honor the obligations of Predix which existed prior to the merger to indemnify Predix s present and former directors and officers. The certificate of incorporation and by-laws of EPIX Delaware, Inc. after the merger provide for the indemnification and elimination of liability for monetary damages to the same extent as set forth in Predix s certificate of incorporation and by-laws and such provision may not be amended, repealed or otherwise modified for a period of six years after the completion of the merger in any manner that would adversely affect the rights of the directors or officers of Predix at the time of the completion of the merger. We have agreed to guarantee the timely payment of all funds owing by, and the timely performance of all obligations of EPIX Delaware, Inc. relating to these indemnification obligations.

**Item 15. *Recent sales of unregistered securities.***

In the three years preceding the filing of this registration statement, we have issued the following securities that were not registered under the Securities Act of 1933, as amended, or the Securities Act:

On December 11, 2006, we issued and sold an aggregate of 3,009,027 shares of our common stock to Glaxo Group Limited and SmithKline Beecham Corporation, doing business as GlaxoSmithKline, for aggregate consideration of approximately \$17.5 million. The shares were offered and sold only to GSK in reliance on Section 4(2) of the Securities Act.

On November 15, 2007, we issued and sold in a private placement 5,245,468 shares of our common stock to a group of institutional and accredited investors at a purchase price of \$3.10 per share for aggregate consideration of approximately \$16.3 million. The shares were offered and sold only to these investors in reliance on Section 4(2) of the Securities Act.

**Item 16. *Exhibits and financial statement schedules.***

(a) *Exhibit Index*

A list of exhibits filed with this registration statement on Form S-1 is set forth on the Exhibit Index and is incorporated in this Item 16(a) by reference.

(b) *Financial Statement Schedules*

None.



**Table of Contents**

**Item 17. *Undertakings.***

The undersigned registrant hereby undertakes:

(a) The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) (§ 230.424(b) of this chapter) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the Calculation of Registration Fee table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment 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.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(b) 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 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 the controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.



**Table of Contents**

**SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, the registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Lexington, Commonwealth of Massachusetts, on March 17, 2008.

EPIX PHARMACEUTICALS, INC.

By: /s/ MICHAEL G. KAUFFMAN, M.D., Ph.D.

Michael G. Kauffman, M.D., Ph.D.  
*Chief Executive Officer*

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities indicated on March 17, 2008:

| <b>Signature</b>   | <b>Title</b>  |
|--|---|
| /s/ MICHAEL G. KAUFFMAN, M.D., Ph.D.<br>Michael G. Kauffman, M.D., Ph.D. | Chief Executive Officer<br>(Principal Executive Officer) and Director   |
| /s/ KIM COBLEIGH DRAPKIN<br>Kim Cobleigh Drapkin, CPA                    | Chief Financial Officer<br>(Principal Financial and Accounting Officer) |
| *  | Chairman of the Board of Directors                                      |
| Frederick Frank  |   |
| *  | Director  |
| Patrick J. Fortune, Ph.D.  |   |
| *  | Director  |
| Michael Gilman, Ph.D.  |   |
| *  | Director  |
| Mark Leuchtenberger  |   |
| *  | Director  |
| Robert J. Perez  |   |
| *  | Director  |

Gregory D. Phelps

\* Director

Ian F. Smith, CPA, ACA

\*By:  
/s/ KIM COBLEIGH DRAPKIN

Kim Cobleigh Drapkin Attorney-in-Fact

II-4

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**Table of Contents****EXHIBIT INDEX**

| <b>Exhibit Number</b> | <b>Description</b>  |
|-----------------------|---|
| 3.1@                  | Restated Certificate of Incorporation of the Company. Filed as Exhibit 3.1 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.   |
| 3.2@                  | Amended and Restated By-Laws of the Company. Filed as Exhibit 3.1 to the Company's Quarterly Report on Form 10-Q for the period ended March 31, 2007 and incorporated herein by reference.  |
| 4.1@                  | Specimen certificate for shares of Common Stock of the Company. Filed as Exhibit 4.1 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.   |
| 4.2@                  | Indenture dated as of June 7, 2004 between the Company and U.S. Bank National Association as Trustee, relating to 3% Convertible Senior Notes due June 15, 2024. Filed as Exhibit 4.1 to the Company's Current Report on Form 8-K filed June 7, 2004 and incorporated herein by reference.  |
| 4.3@                  | Warrant issued to RRD International, LLC. Filed as Exhibit 4.3 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.   |
| 4.4@                  | Warrant issued to General Electric Capital Corporation. Filed as Exhibit 4.4 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.   |
| 5.1**                 | Legal Opinion of Goodwin Procter llp.   |
| 10.1@+                | Amended and Restated License Agreement between the Company and The General Hospital Corporation dated July 10, 1995. Filed as Exhibit 10.14 to the Company's Registration Statement on Form S-1 filed December 10, 1996 (File No. 333-17581) and incorporated herein by reference.  |
| 10.2@#                | Amended and Restated 1992 Incentive Plan. Filed as Appendix A to the Company's 2005 Definitive Proxy Statement on Schedule 14A filed April 29, 2005 and incorporated herein by reference.   |
| 10.3@#                | Form of Incentive Stock Option Certificate. Filed as Exhibit 10.29 to the Company's Registration Statement on Form S-1 filed December 10, 1996 (File No. 333-17581) and incorporated herein by reference.   |
| 10.4@#                | Form of Nonstatutory Stock Option Certificate. Filed as Exhibit 10.30 to the Company's Registration Statement on Form S-1 filed December 10, 1996 (File No. 333-17581) and incorporated herein by reference.  |
| 10.5@#                | Amended and Restated 1996 Director Stock Option Plan. Filed as Appendix B to the Company's 2005 Definitive Proxy Statement on Schedule 14A filed April 29, 2005 and incorporated herein by reference.   |
| 10.6@++               | Amended and Restated Strategic Collaboration Agreement dated as of June 9, 2000, among the Company, Mallinckrodt Inc. (a Delaware corporation) and Mallinckrodt Inc. (a New York corporation). Filed as Exhibit 10.6 to the Company's Annual Report on Form 10-K for the year ended December 31, 2007 and incorporated herein by reference. |
| 10.7@++               | Strategic Collaboration Agreement dated as of June 9, 2000, between the Company and Schering Aktiengesellschaft. Filed as Exhibit 10.7 to the Company's Annual Report on Form 10-K for the year ended December 31, 2007 and incorporated herein by reference.   |
| 10.8@                 | Amendment No. 1 dated as of December 22, 2000 to the Strategic Collaboration Agreement, dated as of June 9, 2000, between the Company and Schering Aktiengesellschaft. Filed as Exhibit 10.8 to the Company's Annual Report on Form 10-K for the period ended December 31, 2007 and incorporated herein by reference.                       |
| 10.9@                 |   |

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Intellectual Property Agreement by and between the Company and Dr. Martin R. Prince, dated November 17, 2003. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed November 18, 2003 and incorporated herein by reference.

10.10@# Description of Director Compensation Arrangements. Filed with the Company's Current Report on Form 8-K filed June 4, 2007 and incorporated herein by reference.

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**Table of Contents**

| <b>Exhibit<br/>Number</b> | <b>Description</b>   |
|---------------------------|--|
| 10.11@#                   | Form of Indemnification Agreement. Filed as Exhibit 10.29 to the Company's Annual Report on Form 10-K for the year ended December 31, 2004 and incorporated herein by reference.   |
| 10.12@                    | Form of Amendment to Stock Option Agreement. Filed as Exhibit 10.30 to the Company's Annual Report on Form 10-K for the year ended December 31, 2004 and incorporated herein by reference.   |
| 10.13@                    | Predix Pharmaceuticals Holdings, Inc. Amended and Restated 2003 Stock Incentive Plan. Filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.   |
| 10.14@                    | Physiome Sciences, Inc. Stock Option Plan (as amended September 21, 2001). Filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.  |
| 10.15@++                  | Amended and Restated License Agreement between Ramot at Tel Aviv University Ltd., Company Registration No. 51-066714-0 and Predix Pharmaceuticals Holdings, Inc., dated as of May 20, 2004. Filed as Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.   |
| 10.16@++                  | Research, Development and Commercialization Agreement between Predix Pharmaceuticals Holdings, Inc. and Cystic Fibrosis Foundation Therapeutics Incorporated, dated as of March 7, 2005. Filed as Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.  |
| 10.17@++                  | License Agreement between Amgen Inc. and Predix Pharmaceuticals Holdings, Inc., dated as of July 31, 2006. Filed as Exhibit 10.5 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.  |
| 10.18@                    | Lease by and between Trustees of 4 Maguire Road Realty Trust and Predix Pharmaceuticals Holdings, Inc., dated as of January 30, 1998, as amended by First Amendment to Lease by and between Trustees of 4 Maguire Road Realty Trust and EPIX Delaware, Inc., dated as of August 31, 2006. Filed as Exhibit 10.6 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference. |
| 10.19@                    | Lease Agreement by and between 150 College Road, LLC and Physiome Sciences, Inc., dated as of December 21, 2000, as amended. Filed as Exhibit 10.7 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.  |
| 10.20@                    | Sublease by and between Predix Pharmaceuticals Holdings, Inc. and Novo Nordisk Pharmaceuticals, Inc., dated as of December 12, 2003. Filed as Exhibit 10.8 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.  |
| 10.21@                    | Unprotected Lease Agreement between Emed Real Estate Development and Investments Company Ltd. and Predix Pharmaceuticals Ltd., dated as of September 26, 2004. Filed as Exhibit 10.9 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.  |
| 10.22@#                   | Predix Pharmaceuticals, Inc. Employment Agreement between Predix Pharmaceuticals, Inc. and Chen Schor, dated as of November 23, 2003. Filed as Exhibit 10.13 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.  |
| 10.23@#                   | Bio-I.T. (Bio Information Technologies) Ltd. Employment Agreement between Bio-I.T. (Bio Information Technologies) Ltd. and Dr. Oren Becker, dated as of October 31, 2000. Filed as Exhibit 10.14 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.  |

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- 10.24@++ Development and License Agreement among SmithKline Beecham Corporation, doing business as GlaxoSmithKline, Glaxo Group Limited and the Company, dated as of December 11, 2006. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K/A filed January 18, 2007 and incorporated herein by reference.
- 10.25@ Stock Purchase Agreement among the Company, Glaxo Group Limited and SmithKline Beecham Corporation, doing business as GlaxoSmithKline, dated as of December 11, 2006. Filed as Exhibit 10.2 to the Company's Current Report on Form 8-K/A filed January 18, 2007 and incorporated herein by reference.
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**Table of Contents**

| <b>Exhibit<br/>Number</b> | <b>Description</b>  |
|---------------------------|---|
| 10.26@                    | First Amendment to License Agreement between Amgen Inc. and the Company, dated as of March 20, 2007. Filed as Exhibit 10.52 to the Company's Annual Report on Form 10-K for the year ended December 31, 2006 and incorporated herein by reference.  |
| 10.27@#                   | Employment Agreement between the Company and Kimberlee C. Drapkin, dated as of March 26, 2007. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed March 29, 2007 and incorporated herein by reference.   |
| 10.28@#                   | Employment Agreement between the Company and Michael G. Kauffman, M.D., Ph.D., dated as of March 27, 2007. Filed as Exhibit 10.2 to the Company's Current Report on Form 8-K filed March 29, 2007 and incorporated herein by reference.   |
| 10.29@#                   | Release Agreement by and between the Company and Oren Becker, dated as of April 5, 2007. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed April 6, 2007 and incorporated herein by reference.  |
| 10.30@#                   | 2006 Employee Stock Purchase Plan. Filed as Appendix A to the Company's 2007 Definitive Proxy Statement on Schedule 14A filed April 30, 2007 and incorporated herein by reference.  |
| 10.31@++                  | First Amendment to Amended and Restated License Agreement between the Company and Ramot at Tel Aviv University Ltd., dated as of June 13, 2007. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed June 15, 2007 and incorporated herein by reference.   |
| 10.32@#                   | Employment Agreement between the Company and Andrew Uprichard, MD, dated as of August 9, 2007. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed August 10, 2007 and incorporated herein by reference.  |
| 10.33@++                  | Third Amendment to Research, Development and Commercialization Agreement between the Company and Cystic Fibrosis Foundation Therapeutics Incorporated, dated as of November 1, 2007. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed November 7, 2007 and incorporated herein by reference. |
| 10.34@                    | Form of Securities Purchase Agreement dated November 9, 2007 between the Company and each of the purchasers listed on Exhibit A thereto. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed November 15, 2007 and incorporated herein by reference.  |
| 10.35@#                   | Form of Restricted Stock Unit Agreement under the Amended and Restated 1992 Incentive Plan. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed February 22, 2008 and incorporated herein by reference.   |
| 10.36@#                   | Form of Restricted Stock Unit Agreement under the Amended and Restated 2003 Stock Incentive Plan. Filed as Exhibit 10.2 to the Company's Current Report on Form 8-K filed February 22, 2008 and incorporated herein by reference.   |
| 12.1@                     | Ratio of Earnings to Fixed Charges. Filed as Exhibit 12.1 to the Company's Annual Report on Form 10-K for the year ended December 31, 2007 and incorporated herein by reference.  |
| 21.1@                     | Subsidiaries of the Company. Filed as Exhibit 21.1 to the Company's Annual Report on Form 10-K for the year ended December 31, 2006 and incorporated herein by reference.   |
| 23.1*                     | Consent of Independent Registered Public Accounting Firm.   |
| 23.2**                    | Consent of Goodwin Procter llp (included in the opinion filed as Exhibit 5.1).  |
| 24.1**                    | Power of Attorney (included on signature page to this Registration Statement).  |

@ Incorporated by reference as indicated.

\* Filed herewith.

- \*\* Previously filed with the initial filing of this Registration Statement on Form S-1 on December 3, 2007.
- # Identifies a management contract or compensatory plan or agreement in which an executive officer or director of the Company participates.
- + Certain confidential material contained in the document has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.
- ++ Certain confidential material contained in the document has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.