EPIX Pharmaceuticals, Inc.
Form 424B3
September 24, 2008

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File No. 333-153204

**PROSPECTUS**

**8,680,120 Shares**

**Common Stock**

This prospectus relates to the resale of up to 8,680,120 in the aggregate of shares of our common stock that we may issue from time to time to the selling stockholder listed in the section beginning on page 30 of this prospectus. The shares of common stock offered under this prospectus by the selling stockholder are issuable to Kingsbridge Capital Limited, or Kingsbridge, pursuant to a common stock purchase agreement between Kingsbridge and ourselves dated August 4, 2008 and a warrant we issued to Kingsbridge on that date. Kingsbridge may be deemed to be an underwriter within the meaning of the Securities Act. We are not selling any securities under this prospectus and will not receive any of the proceeds from the sale of shares by the selling stockholder.

The selling stockholder may sell the shares of common stock described in this prospectus in a number of different ways and at varying prices. We provide more information about how the selling stockholder may sell its shares of common stock in the section titled Plan of Distribution on page 31 of this prospectus. We will not be paying any underwriting discounts or commissions in this offering. We will pay the expenses incurred in registering the shares, including legal and accounting fees.

Our common stock is quoted on the Nasdaq Global Market under the symbol EPIX. The last reported sale price for our common stock on September 23, 2008 was $1.35 per share.

**Investing in our securities involves a high degree of risk. See the section titled Risk Factors on page 7 of this prospectus.**

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

The date of this prospectus is September 24, 2008.

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Unless the context requires otherwise, in this prospectus and the information incorporated herein by reference, the terms EPIX, the Company, we, us, our and similar names refer to EPIX Pharmaceuticals, Inc. and its subsidiarie References to selling stockholder refer to the stockholder listed herein under the heading Selling Stockholder on page 30, who may sell shares from time to time as described in this prospectus.

You should rely only on the information contained or incorporated by reference in this prospectus. We have not, and the selling stockholder has not, authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus is accurate as of the date on the front cover of this prospectus only. Our business, financial condition, results of operations and prospects may have subsequently changed.

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## PROSPECTUS SUMMARY

*The following summary highlights information contained in this prospectus or incorporated by reference. While we have included what we believe to be the most important information about EPIX and this offering, the following summary may not contain all the information that may be important to you. You should read this entire prospectus carefully, including the risks of investing discussed under Risk Factors beginning on page 7, and the information to which we refer you and the information incorporated into this prospectus by reference, for a complete understanding of our business and this offering.*

### Overview

We are a biopharmaceutical company focused on discovering and developing novel therapeutics through the use of our proprietary and highly efficient in silico drug discovery platform. We have a pipeline of internally-discovered drug candidates currently in clinical development to treat diseases of the central nervous system and lung conditions. Our blood-pool imaging agent, Vasovist, is approved for marketing in over 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.

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 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 business strategy is to develop our internally discovered, novel pharmaceutical product candidates through the point of proof of clinical concept, typically completion of Phase 2 clinical trials, and then to seek third-party collaborators for their continued development, regulatory approval and commercialization. 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 certain commercialization rights. In March 2008, we discontinued development of one of our clinical-stage programs, PRX-00023, due to lack of efficacy shown in a recently completed Phase 2b trial in patients with major depressive disorder.

### Our Product Candidates

We currently have one imaging product, Vasovist, which is approved for marketing in more than 30 countries outside of the United States. In January 2008, based on written confirmation from the U.S. Food and Drug Administration, or FDA, regarding our protocol design and statistical analysis plan, we initiated a re-read of the images obtained in prior Phase 3 studies of Vasovist. In April 2008, we announced that we achieved statistically significant positive results from the blinded, independent re-read and had met all pre-specified endpoints prospectively agreed to with the FDA. As a result, we resubmitted a New Drug Application, or NDA, to the FDA for Vasovist on June 30, 2008. In July

2008, we received written confirmation from the FDA that our NDA was a complete submission and that the FDA set a user fee goal date of December 31, 2008 for our NDA.

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The following summarizes the applicable disease indication and the clinical status of our three current clinical-stage therapeutic drug candidates:

| Drug Candidate | Disease Indication | Clinical Trial Status |
|---|---|---|
| PRX-03140(1) | Alzheimer s disease | Phase 2b |
| PRX-08066(2) | Pulmonary Hypertension/COPD | Phase 2b |
| PRX-07034(3) | Cognitive impairment | Phase 1b |

(1) In May 2008, we initiated a Phase 2b trial in Alzheimer s disease of PRX-03140 in combination with donepezil (Aricept®). This randomized, double-blind, placebo-controlled trial is designed to evaluate the efficacy of PRX-03140 on cognitive function as measured by the change from baseline in the cognitive component of the Alzheimer s Disease Assessment Scale (ADAS-Cog) score. Patients will be randomized to one of three trial arms: placebo, 50 mg of PRX-03140 once daily or 150 mg of PRX-03140 once daily. All patients in the trial must be treated with 10 mg of Aricept® for at least four months prior to enrollment. The six month trial is expected to enroll approximately 420 adult patients with Alzheimer s disease.

In May 2008, we initiated a second Phase 2b trial of PRX-03140 as monotherapy treatment of Alzheimer s disease. This randomized, double-blind, placebo-controlled trial is designed to evaluate the efficacy of PRX-03140 on cognitive function as measured by the change from baseline in the ADAS-Cog score. Patients will be randomized to one of four trial arms: placebo, donepezil (Aricept®) positive control, 50 mg of PRX-03140 once daily or 150 mg of PRX-03140 once daily. The three month trial is expected to enroll approximately 240 adult patients with Alzheimer s disease. This monotherapy trial will also include a three month optional extension.

(2) We completed a Phase 2a trial of PRX-08066 in pulmonary hypertension associated with chronic obstructive pulmonary disease, or COPD, in August 2007. This randomized, double-blind, placebo-controlled Phase 2 trial enrolled 71 patients with PH associated with COPD. Patients were randomized to one of three arms: 200 mg of PRX-08066 once-daily, 400 mg of PRX-08066 once-daily or placebo. The two-week double-blind phase of the study was followed by an open label extension in which 10 patients received 200 mg daily for six weeks. The primary endpoints of the trial were safety and tolerability of PRX-08066. Efficacy was measured by the effect of PRX-08066 compared to placebo on systolic pulmonary artery pressure, or SPAP, and included 62 evaluable patients who completed the double-blind portion of the study. In a population where decreases of 3 mmHg to 4 mmHg in a post-exercise SPAP are considered clinically significant, the results showed a statistically significant dose-response for the patients that demonstrated a decrease of 4 mmHg or more. In the 400 mg dose group, 45% of the patients had a reduction in post-exercise SPAP of 4 mmHg or more versus 14% on placebo (p=0.043). An analysis of SPAP changes in all subjects revealed a dose trend with median reductions of 1.2 mmHg and 3.38 mmHg in the 200 mg and 400 mg dose groups, respectively, compared with no change on placebo. PRX-08066 was generally well-tolerated. There were no serious adverse events considered related to PRX-08066, and the majority of adverse events were mild or moderate in nature. One subject in the 200 mg dose group who then continued into the six-week open-label extension experienced a modest increase in liver enzyme levels at the end of the extension that was believed to be drug-related. These values returned to normal within two weeks and the subject remained asymptomatic.

In August 2008, we initiated a Phase 2b right-heart catheter study of PRX-08066 in patients with chronic obstructive pulmonary disease and moderate-to-severe pulmonary hypertension. The single-arm, open-label study is designed to evaluate the mean pulmonary artery blood pressure change from baseline as measured directly by

right-heart catheterization and will also measure the change from baseline in the standard six-minute walk distance test after three months of treatment. Patients will be treated with 500 mg of PRX-08066 on day one of the trial followed by twice-daily dosing of 300 mg of PRX-08066 for three months.

(3) In October 2007, we completed a randomized, double-blind, placebo-controlled Phase 1 trial of 21 healthy obese adults. Findings from this study demonstrated that adults taking 600 mg of PRX-07034 twice-daily for 28 days had a weight reduction of an average of 0.45 kg (approximately 1 pound), while adults on placebo gained 1.37 kg (approximately 3 pounds) during the same period, which was statistically

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significant ($p < 0.005$). PRX-07034 appeared well-tolerated and there were no serious adverse events reported. An increase in corrected QT interval, or QTc, was apparent at the dose tested, however, with a mean increase over the duration of the study of 10.7 milliseconds for the drug group versus a decrease of 1.7 milliseconds for the placebo group. The corrected QTc is a measurement of the QT interval, which is corrected for heart rate. Prolongations of the QTc are associated with an increased risk for potentially life-threatening heart rhythms and so this measurement is an important index to measure during the development of new drugs. In addition, of the population of 21 adults, one patient on drug discontinued due to a rash that resolved rapidly. There were no discontinuations on placebo. In the prior Phase 1 trial where doses up to 600 mg once daily were studied for 28 days, no clinically meaningful prolongations of the QTc were noted.

**Risks Affecting Us**

You should carefully consider the matters discussed in the section Risk Factors beginning on page 7, 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.

**Corporate Information**

We were organized as a Delaware corporation in 1988 and commenced operations in 1992. Our principal executive offices are located at 4 Maguire Road, Lexington, Massachusetts 02421. Our telephone number at that location is (781) 761-7600. Our website is located at www.epixpharma.com. We make available on our website free of charge a link to our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports as soon as practicable after we electronically file such material with the Securities and Exchange Commission ( SEC ). The information contained on our website is not part of this prospectus.

**Equity Financing with Kingsbridge Capital**

On August 4, 2008, we entered into a Committed Equity Financing Facility, or CEFF, with Kingsbridge, pursuant to which Kingsbridge committed to purchase, subject to certain conditions, up to the lesser of $50 million or 8,280,120 shares of our common stock. In connection with the CEFF, we entered into a common stock purchase agreement and registration rights agreement with Kingsbridge, both dated August 4, 2008, and on that date we also issued a warrant to Kingsbridge to purchase 400,000 shares of our common stock at a price of $2.4925 per share. This warrant is fully exercisable beginning six months after August 4, 2008 and for a period of five years thereafter.

The shares of common stock that may be issued to Kingsbridge under the common stock purchase agreement and the warrant will be issued pursuant to an exemption from registration under the Securities Act of 1933, as amended, or the Securities Act. Pursuant to the registration rights agreement, we have filed a registration statement of which this prospectus is a part, covering the possible resale by Kingsbridge of any shares that we may issue to Kingsbridge under the common stock purchase agreement or upon exercise of the warrant. Through this prospectus, Kingsbridge may offer to the public for resale shares of our common stock that we may issue to Kingsbridge pursuant to the common stock purchase agreement, or that Kingsbridge may acquire upon exercise of the warrant.

The common stock purchase agreement entitles us to sell and obligates Kingsbridge to purchase, from time to time over a period of three years from the first trading day following the effectiveness of the registration statement of which this prospectus is a part, shares of our common stock for cash consideration up

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to an aggregate of the lesser of $50 million or 8,280,120 shares of our common stock, subject to certain conditions and restrictions. We may, from time to time, at our discretion, and subject to certain conditions that we must satisfy, draw down funds under the CEFF by selling shares of our common stock to Kingsbridge. The purchase price of these shares will be at a discount ranging from six to twelve percent of the volume weighted average of the price of our common stock for each of the eight trading days following our election to sell shares, or draw down under the CEFF. The discount on each of these eight trading days will be determined as follows, and the resultant price will be used to determine the number of shares issuable to Kingsbridge with respect to one-eighth (1/8) of the aggregate draw down amount:

| VWAP* | Percent of VWAP | (Applicable Discount) |
|---|---|---|
| Greater than $10.00 per share | 94% | (6)% |
| Less than or equal to $10.00 per share but greater than $5.00 per share | 92% | (8)% |
| Less than or equal to $5.00 per share but greater than $1.90 per share | 90% | (10)% |
| Less than or equal to $1.90 per share but greater than or equal to $1.25 per share | 88% | (12)% |

* As set forth in the common stock purchase agreement, VWAP means the volume weighted average price (the aggregate sales price of all trades of our common stock during each trading day divided by the total number of shares of common stock traded during that trading day) of our common stock during any trading day as reported by Bloomberg, L.P. using the AQR function. The VWAP and corresponding discount will be determined for each of the eight trading days during a draw down pricing period.

During the eight trading day pricing period for a draw down, if the VWAP for any one trading day is less than the greater of (i) $1.25 or (ii) 90 percent of the closing price of our common stock for the trading day immediately preceding the beginning of the draw down period, the VWAP from that trading day will not be used in calculating the number of shares to be issued in connection with that draw down, and the draw down amount for that pricing period will be reduced by one-eighth (1/8) of the draw down amount we had initially specified. In addition, if trading in our common stock is suspended for any reason for more than three consecutive or non-consecutive hours during any trading day during a draw down pricing period, that trading day will not be used in calculating the number of shares to be issued in connection with that draw down, and the draw down amount for that pricing period will be reduced by one eighth (1/8) of the draw down amount we had initially specified.

The maximum number of shares of common stock that we can issue pursuant to the CEFF is 8,280,120 shares. An additional 400,000 shares of common stock are issuable if Kingsbridge exercises the warrant that we issued to it in connection with its entry into the CEFF. We intend to exercise our right to draw down amounts under the CEFF, if and to the extent available, at such times as we have a need for additional capital and when we believe that sales of stock under the CEFF provide an appropriate means of raising capital.

Our ability to require Kingsbridge to purchase our common stock is subject to various limitations. We can make draw downs of a maximum amount of, at our discretion, either (i) 1.5 percent of our market capitalization at the time of the draw down, or (ii) the lesser of (A) 3.0 percent of our market capitalization at the time of the draw down and (B) the alternative draw down amount calculated pursuant to the common stock purchase agreement. Neither (i) nor (ii) may exceed a $10 million limit. Unless Kingsbridge agrees otherwise, a minimum of three trading days must elapse between the expiration of any draw down pricing period and the beginning of the next draw down pricing period. Kingsbridge is not obligated to purchase shares at prices below $1.25 per share.

During the term of the CEFF, without Kingsbridge s prior written consent, we may not issue securities that are, or may become, convertible or exchangeable into shares of common stock where the purchase, conversion or exchange price for our common stock is determined using a floating discount or other post-issuance adjustable discount to the market price of the common stock, including pursuant to an equity line or other financing that is substantially similar to the arrangement provided for in the CEFF, with certain exceptions.

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The issuance of our common stock under the CEFF or upon exercise of the Kingsbridge warrant will have no effect on the rights or privileges of existing holders of common stock except that the economic and voting interests of each stockholder will be diluted as a result of the issuance. Although the number of shares of common stock that stockholders presently own will not decrease, these shares will represent a smaller percentage of our total shares that will be outstanding after any issuances of shares of common stock to Kingsbridge. If we draw down amounts under the CEFF when our share price is decreasing, we will need to issue more shares to raise the same amount than if our stock price was higher. Such issuances will have a dilutive effect and may further decrease our stock price.

Kingsbridge agreed in the common stock purchase agreement that during the term of the CEFF, neither Kingsbridge nor any of its affiliates, nor any entity managed or controlled by it, will enter into any short sale of any shares of our common stock as defined in Regulation SHO promulgated under the Securities Exchange Act of 1934, as amended, or the Exchange Act.

Before Kingsbridge is obligated to buy any shares of our common stock pursuant to a draw down, the following conditions, none of which is in Kingsbridge s control, must be met:

Each of our representations and warranties in the common stock purchase agreement shall be true and correct in all material respects as of the date when made and as of the draw down exercise date as though made at that time, except for representations and warranties that are expressly made as of a particular date.

We shall have performed, satisfied and complied in all material respects with all covenants, agreements and conditions required by the common stock purchase agreement, the registration rights agreement and the warrant to be performed, satisfied or complied with by us.

We shall have complied in all respects with all applicable federal, state and local governmental laws, rules, regulations and ordinances in connection with the execution, delivery and performance of the common stock purchase agreement and the consummation of the transactions it contemplates, except for any failures to so comply which could not be reasonably expected to have a material adverse effect on us.

The registration statement, which includes this prospectus, shall have previously become effective and shall remain effective and neither we nor the selling stockholder shall have received notice that the Securities and Exchange Commission, or the SEC, has issued or intends to issue a stop order with respect to the registration statement or that the SEC otherwise has suspended or withdrawn the effectiveness of the registration statement, either temporarily or permanently, or intends or has threatened to do so (unless the SEC s concerns have been addressed and the selling stockholder is reasonably satisfied that the SEC no longer is considering or intends to take such action), and (ii) no other suspension of the use or withdrawal of the effectiveness of the registration statement or this prospectus shall exist.

We shall not have knowledge of any event that could reasonably be expected to have the effect of causing the registration statement applicable to Kingsbridge s resale of shares of our common stock to be suspended or otherwise ineffective.

Trading in our common stock shall not have been suspended by the SEC, the Nasdaq Global Market or the Financial Industry Regulatory Authority and trading in securities generally on the Nasdaq Global Market shall not have been suspended or limited.

No statute, rule, regulation, order, decree, writ, ruling or injunction shall have been enacted, entered, promulgated or endorsed by any court or governmental authority which prohibits the consummation of any of the transactions contemplated by the common stock purchase agreement.

No action, suit or proceeding before any arbitrator or any court or governmental authority shall have been commenced or, to our knowledge, threatened, and to our knowledge no inquiry or investigation by any governmental authority shall have been threatened against us or any of our officers, directors or

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affiliates seeking to enjoin, prevent or change the transactions contemplated by the common stock purchase agreement or seeking damages in connection with such transactions.

We shall have sufficient shares of common stock, calculated using the closing trade price of the common stock as of the trading day immediately preceding a draw down, registered under the registration statement to issue and sell such shares in accordance with such draw down.

The warrant to purchase 400,000 shares of our common stock shall have been duly executed, delivered and issued to Kingsbridge, and we shall not be in default in any material respect under the warrant.

Kingsbridge shall have received an opinion from our outside legal counsel in the form previously agreed to.

There is no guarantee that we will be able to meet the foregoing conditions or any other conditions under the common stock purchase agreement or that we will be able to draw down any portion of the amounts available under the CEFF.

We also entered into a registration rights agreement with Kingsbridge. Pursuant to the registration rights agreement, we have filed a registration statement, which includes this prospectus, with the SEC relating to Kingsbridge s resale of any shares of common stock purchased by Kingsbridge under the common stock purchase agreement or issued to Kingsbridge as a result of the exercise of the Kingsbridge warrant. The effectiveness of this registration statement is a condition precedent to our ability to sell common stock to Kingsbridge under the common stock purchase agreement. We are entitled in certain circumstances, including the existence of certain kinds of nonpublic information, to deliver a blackout notice to Kingsbridge to suspend the use of this prospectus and prohibit Kingsbridge from selling shares under this prospectus. If we deliver a blackout notice in the 15 trading days following the settlement of a draw down, or if the registration statement of which this prospectus is a part is not effective in circumstances not permitted by the registration rights agreement, then we must pay amounts to Kingsbridge, or issue Kingsbridge additional shares in lieu of payment, calculated by means of a varying percentage of an amount based on the number of shares held by Kingsbridge that were purchased pursuant to such draw down and the change in the market price of our common stock between the date the blackout notice is delivered (or the registration statement is not effective) and the date the prospectus again becomes available.

Kingsbridge may, upon one business day s notice to us, terminate the CEFF if we enter into a transaction prohibited by the common stock purchase agreement without Kingsbridge s prior written consent or within ten trading days after Kingsbridge provides notice to us of a material adverse event relating to our business. Kingsbridge may also terminate the CEFF upon one business day s notice to us at any time in the event that a registration statement is not initially declared effective in accordance with the registration rights agreement. We may terminate the CEFF upon one business day s notice to Kingsbridge, except that we may not terminate the CEFF during any draw down pricing period. In addition, either we or Kingsbridge may terminate the CEFF upon one day s notice if the other party has breached a material representation, warranty or covenant to the common stock purchase agreement and such breach is not remedied within ten trading days after notice of such breach is delivered to the breaching party.

The foregoing summary of the CEFF does not purport to be complete and is qualified by reference to the common stock purchase agreement, the registration rights agreement and the warrant, copies of which have been filed as exhibits to the registration statement of which this prospectus is a part.

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## RISK FACTORS

*We operate in a rapidly changing environment that involves a number of risks, some of which are beyond our control. This discussion highlights some of the risks which may affect future operating results. These are the risks and uncertainties we believe are most important for you to consider. 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 business in general, may also impair our business operations. If any of the following risks or uncertainties actually occurs, our business, financial condition and operating results would likely suffer.*

### 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 June 30, 2008 were approximately $424.2 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;

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

the costs of developing marketing and distribution capabilities.

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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 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 focused our development efforts for this product candidate in depression. In March 2008, we discontinued development of PRX-00023 due to lack of efficacy shown in a recently completed Phase 2b trial in patients with major depressive disorder.

In addition, each of our current clinical-stage therapeutic 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 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

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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 six months ended June 30, 2008 was $19.8 million and consisted of $18.8 million of product development revenue from, GlaxoSmithKline,CFFT and Bayer Schering Pharma AG, Germany, $0.3 million of royalty revenue related to the Bayer Schering Pharma AG, Germany agreements, and $0.7 million of license fee revenue related to the GlaxoSmithKline, CFFT, Bayer Schering Pharma AG, Germany and Covidien, 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 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,

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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, or terminate, our ongoing and planned clinical trials for our product candidates and negatively impact our 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;

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delay in developing, or our inability to obtain, 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 or termination of a clinical program;

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-03140, our product candidate for the treatment of Alzheimer s disease, could be significant. Achieving primary efficacy endpoints in clinical trials can be difficult in certain disease areas due to the placebo effect commonly observed in trials in certain patient populations. For example, our results from the completed Phase 3 and Phase 2b clinical studies of PRX-00023 in September 2006 and March 2008 indicated that PRX-00023 did not achieve a statistically significant improvement over placebo for their respective primary endpoints with respect to generalized anxiety disorder and major depressive disorder. Therefore, we discontinued our development efforts with respect to PRX-00023.

***Despite our resubmission of a new drug application with the FDA for Vasovist, we may never obtain approval to market and sell Vasovist in the United States or monetize the potential royalty stream therefrom, either of which would materially harm our revenues.***

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 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, and in April 2008 we announced that we met all pre-specified endpoints for the re-read prospectively agreed to with the FDA. Although we resubmitted an NDA to the FDA for Vasovist on June 30, 2008, the approval and labeling of Vasovist remains subject to

significant uncertainties related to a number of factors, including the FDA s review process and conclusions regarding the NDA resubmission. We cannot assure you that the FDA will approve Vasovist. If the FDA does not approve Vasovist, we will not receive revenues based on sales of Vasovist in the United States.

In addition, pursuant to our collaboration with Bayer Schering Pharma AG, Germany, we are entitled to a percentage of Bayer Schering Pharma AG, Germany s operating profit margin on sales of Vasovist in the United States. We may seek to monetize these potential royalties to fund our clinical pipeline. Any failure or delay by the FDA in approving Vasovist could materially and adversely affect our ability to enter into any such agreements. In addition, our ability to successfully monetize our interest in sales of Vasovist in the United States will also be dependent on current and historical sales of Vasovist by Bayer Schering Pharma AG, Germany outside the United States. To date, sales of Vasovist outside the United States have not been significant. We cannot assure you that we would be able to enter into an agreement with a third party to monetize such royalties, and our failure to do so could materially and adversely affect our ability to generate revenues. In addition, disagreements with Bayer Schering Pharma AG, Germany regarding our collaboration or otherwise could delay or terminate our efforts to successfully monetize our share of U.S. royalties on Vasovist.

***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-03140, PRX-08066 and PRX-07034 in December 2004, May 2005 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 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

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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 recently completed Phase 2b clinical trial of PRX-00023 in major depressive disorder in March 2008, which was designed to evaluate the efficacy of PRX-00023 as measured by the change from baseline in the Montgomery Asberg Depression Rating Scale compared to placebo, demonstrated that PRX-00023 did not achieve a statistically significant improvement over placebo for the primary endpoint with respect to major depressive disorder. Based on these results, we have discontinued our development efforts of PRX-00023. 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. Certain of our preclinical and clinical product candidates have in the past and may in the future demonstrate safety concerns. 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.

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***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);

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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-03140, PRX-08066 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

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, Australia and South Korea,, 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

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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-03140, PRX-08066 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.

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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-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. 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

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OptiMARK by Covidien Ltd. We are aware of six 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. s 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.

***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 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-03140, PRX-08066 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.

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***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 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. There can be no assurance that we will be able to retain any of our key management and scientific personnel. Each of our executive officers and key scientific personnel could terminate his or her relationship with us at any time. For instance, in May 2008, Andrew Uprichard, M.D. resigned his position as our President, and, in July 2008, Michael G. Kauffman, M.D., Ph.D. resigned his position as our Chief Executive Officer. Drs. Uprichard and Kauffman have been critical to the pursuit of our business goals and we may experience difficulties implementing our business strategy following their respective departures. 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 additional key employees, 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, 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.

***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

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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 August 18, 2008, our patent portfolio included a total of 15 issued U.S. patents, 122 issued foreign patents, and 270 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 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-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 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 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**

***If we do not maintain effectiveness of the registration statement 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

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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.

***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 June 30, 2007 to August 25, 2008, the closing price of our common stock ranged from $1.32 to $5.86 per share. The last reported closing price for our common stock on August 25, 2008 was $1.84. 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.

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***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 RELATED TO THE COMMITTED EQUITY FINANCING FACILITY WITH KINGSBRIDGE**

***The Committed Equity Financing Facility that we entered into with Kingsbridge may not be available to us if we elect to make a draw down, may require us to make additional blackout or other payments to Kingsbridge, and may result in dilution to our stockholders.***

In August 2008, we entered into the CEFF with Kingsbridge. The CEFF entitles us to sell and obligates Kingsbridge to purchase, from time to time over a period of three years, shares of our common stock for cash consideration, subject to certain conditions and restrictions. Kingsbridge will not be obligated to purchase shares under the CEFF unless certain conditions are met, which include a minimum price for our common stock; the accuracy of representations and warranties made to Kingsbridge; compliance with laws; effectiveness of the registration statement of which this prospectus is a part; and the continued listing of our stock on the Nasdaq Global Market. In addition, Kingsbridge is permitted to terminate the CEFF if it determines that a material and adverse event has occurred affecting our business, operations, properties or financial condition and if such condition continues for a period of ten days from the date Kingsbridge provides us notice of such material and adverse event. If we are unable to access funds through the CEFF, or if the CEFF is terminated by Kingsbridge, we may be unable to access capital on favorable terms or at all.

We are entitled in certain circumstances to deliver a blackout notice to Kingsbridge to suspend the use of the registration statement of which this prospectus is a part and prohibit Kingsbridge from selling shares under this prospectus. If we deliver a blackout notice in the 15 trading days following the settlement of a draw down, or if the registration statement is not effective in circumstances not permitted by the agreement, then we must make a payment to Kingsbridge, or issue Kingsbridge additional shares in lieu of this payment, calculated on the basis of the number of shares held by Kingsbridge (exclusive of shares that Kingsbridge may hold pursuant to exercise of the Kingsbridge warrant) and the change in the market price of our common stock during the period in which the use of the registration statement is suspended. If the trading price of our common stock declines during a suspension of the registration statement, the blackout or other payment could be significant.

Should we sell shares to Kingsbridge under the CEFF, or issue shares in lieu of a blackout payment, it will have a dilutive effective on the holdings of our current stockholders, and may result in downward pressure on the price of our common stock. If we draw down under the CEFF, we will issue shares to Kingsbridge at a discount of up to twelve percent from the volume weighted average price of our common stock. If we draw down amounts under the CEFF

when our share price is decreasing, we will need to issue more shares to raise the same amount than if our stock price was higher. Issuances in the face of a declining share price will have an even greater dilutive effect than if our share price were stable or increasing, and may further decrease our share price.

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## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and any accompanying prospectus supplement (including any document incorporated by reference herein or therein) contain statements with respect to the Company which constitute forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. and of the safe harbor provisions of the United States Private Securities Litigation Reform Act of 1995. Words such as anticipate, believes, budget, continue, could, estimate, expect, forecast, in potential, predicts, project, should, will and similar expressions are intended to identify such forward-looking statements. Forward-looking statements involve inherent risks and uncertainties, which are difficult to predict and many of which are beyond our control. A number of important factors could cause actual results to differ materially from those in the forward-looking statements, including those factors discussed in Risk Factors in any prospectus supplement and in the documents incorporated by reference herein or therein. Factors that could cause actual results to differ from those reflected in forward-looking statements relating to our operations and business include:

- 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.

We caution readers not to place undue reliance on any such forward-looking statements, which speak only as of the date they are made. We disclaim any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such statements to reflect any change in company expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

You should read this prospectus and any accompanying prospectus supplement and the documents that we reference herein and therein and have filed as exhibits to the registration statement, of which this prospectus is part, completely and with the understanding that our actual future results may be materially different from what we expect. You should assume that the information appearing in this prospectus and any accompanying prospectus supplement is accurate as of the date on the front cover of this prospectus or such prospectus supplement only. Our business, financial condition, results of operations and prospects may change. We may not update these forward-looking statements, even though our situation may change in the future, unless we have obligations under the Federal securities laws to update and disclose material developments related to previously disclosed information. We qualify all of the information presented in this prospectus and any accompanying prospectus supplement, and particularly our forward-looking statements, by these cautionary statements.

## USE OF PROCEEDS

We will not receive any of the proceeds from the sale of shares of our common stock by the selling stockholder pursuant to this prospectus. Any issuance of shares by us to Kingsbridge under the common stock purchase agreement or in connection with the exercise of the Kingsbridge warrant will be made pursuant to an exemption from the registration requirements of the Securities Act. To the extent the warrant held by the selling stockholder is exercised at its current exercise price, we would receive approximately $977,000 in cash proceeds, unless such warrant is exercised on a cashless basis pursuant to its terms.

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Unless otherwise provided in the applicable prospectus supplement, we intend to use the proceeds from our sales, if any, to Kingsbridge for general corporate purposes, which may include funding clinical trials, research and development, regulatory activities and product marketing, repayment or refinancing of existing indebtedness, investments, capital expenditures, and acquisitions of companies, products, intellectual property or other technology. We may also invest the net proceeds temporarily in short-term or marketable securities until we use them for their stated purpose.

## SELLING STOCKHOLDER

This prospectus relates to the possible resale by the selling stockholder, Kingsbridge, of shares of common stock that we may issue pursuant to the common stock purchase agreement we entered into with Kingsbridge on August 4, 2008, or upon exercise of the warrant we issued to Kingsbridge. We are filing the registration statement of which this prospectus is a part pursuant to the provisions of the registration rights agreement we entered into with Kingsbridge on August 4, 2008.

The selling stockholder may from time to time offer and sell pursuant to this prospectus any or all of the shares that it acquires under the common stock purchase agreement or upon exercise of the warrant.

The following table presents information regarding Kingsbridge and the shares that it may offer and sell from time to time under this prospectus. This table is prepared based on information supplied to us by the selling stockholder. As used in this prospectus, the term selling stockholder includes Kingsbridge and any donees, pledges, transferees or other successors in interest selling shares received after the date of this prospectus from a selling stockholder as a gift, pledge or other non-sale related transfer. The number of shares in the column Number of Shares Being Offered represents all of the shares that the selling stockholder may offer under this prospectus. The selling stockholder may sell some, all or none of its shares. We do not know how long the selling stockholder will hold the shares before selling them, and we currently have no agreements, arrangements or understandings with the selling stockholder regarding the sale of any of the shares.

Beneficial ownership is determined in accordance with Rule 13d-3(d) promulgated by the SEC under the Exchange Act. The percentage of shares beneficially owned prior to the offering is based both on 41,421,315 shares of our common stock actually outstanding as of August 1, 2008 and on the assumption that all shares of common stock issuable under the common stock purchase agreement we entered into with Kingsbridge on August 4, 2008 and all shares of common stock issuable upon exercise of the warrant held by Kingsbridge are outstanding as of that date.

| | | **Shares of Common Stock Beneficially Owned Prior to the Offering** | | **Shares of Common Stock Beneficially Owned After Offering** |
|---|---|---|---|---|
| **Security Holders** | &nb | | **Number of Shares** | |