

EPIX Pharmaceuticals, Inc.  
Form 10-K  
March 13, 2009

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

**Form 10-K**

(Mark One)

- ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**  
**For the fiscal year ended December 31, 2008**
- OR**
- TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**  
**For the transition period from        to**

**Commission file number: 0-21863**

**EPIX PHARMACEUTICALS, INC.**

*(Exact name of registrant as specified in its charter)*

**Delaware**

*(State or other jurisdiction of  
incorporation or organization)*

**4 Maguire Road, Lexington, Massachusetts**

*(Address of principal executive offices)*

**04-3030815**

*(I.R.S. Employer  
Identification No.)*

**02421**

*(Zip Code)*

**Registrant's telephone number, including area code:**

**(781) 761-7600**

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

**Title of Each Class**

**Name of Each Exchange on Which Registered**

Common Stock, \$0.01 par value per share

The NASDAQ Stock Market LLC

**Securities registered pursuant to Section 12(g) of the Exchange Act:**

**NONE**

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

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

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

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

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

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

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

The aggregate market value of the registrant's voting and non-voting common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) computed by reference to the price at which the common stock was last sold as of the last business day of the registrant's most recently completed second fiscal quarter was \$63.1 million.

As of March 10, 2009, the registrant had 41,947,441 shares of common stock outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE**

The following documents (or parts thereof) are incorporated by reference into the following parts of this Form 10-K: Certain information required in Part III of this Annual Report on Form 10-K is incorporated from the Registrant's Proxy Statement for the 2009 Annual Meeting of Stockholders.

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Our name and corporate logo are trademarks of EPIX Pharmaceuticals, Inc. All other trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners.

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**PART I**

*This Annual Report on Form 10-K contains 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 are subject to the safe harbor created by those sections. These statements relate to, among other things, our expectations concerning our research and development efforts, regulatory compliance, commercial strategy, strategic alliances and collaborative efforts and their likely future success. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. Some of the forward-looking statements can be identified by the use of forward-looking terms such as believes, expects, may, will, should, seek, intends, plans, estimates, anticipates, or other comparable terms. Accordingly, these statements involve estimates, assumptions and uncertainties that could cause actual results to differ materially from those expressed in them. Our actual results may differ significantly from the results discussed in the forward-looking statements. Factors that might cause such a difference include, but are not limited to, those set forth in Item 1A. Risk Factors and elsewhere in this Annual Report on Form 10-K. We have no plans to update our forward-looking statements to reflect events or circumstances after the date of this report. We caution readers not to place undue reliance upon any such forward-looking statements, which speak only as of the date made.*

**ITEM 1. BUSINESS**

**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. We also have collaborations with SmithKline Beecham Corporation (GlaxoSmithKline), Amgen Inc., and Cystic Fibrosis Foundation Therapeutics, Incorporated, or CFFT. Our business strategy is to develop our internally discovered, novel pharmaceutical products through the point of proof of clinical concept, typically completion of Phase 2 clinical trials and then to seek pharmaceutical partnerships for the continued development, regulatory approvals and world-wide commercialization of the product candidates. In certain disease areas, such as pulmonary hypertension, where we believe we can efficiently obtain regulatory approval and effectively market the product through a specialty sales force, we may seek to retain commercialization rights in the United States.

Since our acquisition of Predix Pharmaceuticals Holdings, Inc., or Predix, in August 2006, our focus has been on the development of therapeutic drug products. 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 typically 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 blood-pool magnetic resonance angiography imaging agent, Vasovist, was approved by the U.S. Food and Drug Administration, or FDA, for marketing in the United States in December 2008, and has been approved for marketing in over 30 countries outside of the United States. In September 2008, Bayer Schering Pharma AG, Germany, or Bayer Schering, terminated the strategic collaboration agreement between us and Bayer Schering relating to Vasovist, effective March 1, 2009. Accordingly, the worldwide commercial rights

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for Vasovist were transferred back to us on such date. It is our intention to sell the commercial rights to Vasovist. However, there is no guarantee that we will be able to do so. Upon a sale of the commercial rights to Vasovist, we will be required to reimburse Bayer Schering for a portion of their development costs. The reimbursement will be based on pre-defined percentages of the development costs, allocated to each territory for which the commercial rights are sold, with full worldwide rights amounting to a \$33 million reimbursement to Bayer Schering.

We have experienced and continue to experience negative cash flows from operations and we expect to continue to incur net losses in the foreseeable future. Accordingly, in March 2009 and October 2008, we implemented workforce reductions that eliminated approximately 62% of our workforce in connection with our efforts to reduce our cost structure. We also narrowed the focus of our research and development efforts to our lead clinical programs, PRX-03140 being developed for the treatment of Alzheimer's disease and PRX-08066 being developed for the treatment of pulmonary hypertension associated with chronic obstructive pulmonary disease (COPD), as well as our partnered preclinical programs with GlaxoSmithKline and CFRT. In connection with the March 2009 workforce reduction, we entered into a letter agreement with GlaxoSmithKline allowing us to reduce our research and development obligations under our collaboration agreement, during the period from March 13, 2009 to September 13, 2009, for programs other than the PRX-03140 program.

As of December 31, 2008, we had \$24.6 million of cash and cash equivalents to fund our future operations. We believe that our cash and cash equivalents, along with anticipated revenue that we expect to earn during the first half of 2009, will fund our operations only through the end of August 2009. In addition, on February 4, 2009, we received notice from the Listing Qualifications Panel of the NASDAQ Stock Market LLC, or NASDAQ, that it has determined to continue the listing of our common stock on the NASDAQ Global Market subject to our compliance with Marketplace Rule 4450(b)(1)(A), which requires us to maintain a market value of our common stock of at least \$50,000,000 for at least 10 consecutive days on or prior to May 11, 2009. As of March 10, 2009, we were not in compliance with the requirement for continued inclusion on NASDAQ. If we do not regain compliance with the rules for continued listing on NASDAQ, our common stock will be delisted from NASDAQ. If our common stock is delisted from NASDAQ, the holders of our \$100 million aggregate principal amount of 3% Convertible Senior Notes could redeem their notes at face value, plus accrued and unpaid interest. We currently do not have sufficient funds to repurchase more than a nominal amount of the notes if tendered by the holders. Accordingly, we will need to raise significant additional capital to fund our operations beyond August 2009 or if we are required to redeem the notes. If we are unable to obtain such additional capital, we will not be able to sustain our operations and would be required to cease our operations and/or seek bankruptcy protection. Given the difficult current economic environment, we believe that it will be difficult to raise additional funds and there can be no assurance as to the availability of additional financing or the terms upon which additional financing may be available. As a result of our recurring operating losses and need for additional financing, the audit report relating to our consolidated financial statements for the year ended December 31, 2008 contains an explanatory paragraph regarding our ability to continue as a going concern.

Throughout this Annual Report on Form 10-K, except where otherwise stated or indicated by the context, we, us, or our means EPIX Pharmaceuticals, Inc. and its consolidated subsidiaries and their predecessors (including Predix).

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**OUR CLINICAL PRODUCT CANDIDATES**

The following chart summarizes the status of our clinical drug development programs as of March 10, 2009:

Through the application of our GPCR and ion channel drug discovery expertise, over the past five years we have created a pipeline of drug candidates designed to address diseases with significant unmet medical needs and commercial potential across a range of therapeutic areas.

*PRX-03140 for Alzheimer's disease*

PRX-03140 is a novel, highly selective, small-molecule 5-HT<sub>4</sub> agonist that we are developing for the treatment of Alzheimer's disease. PRX-03140 is being developed to provide improved cognition and to potentially slow Alzheimer's disease progression. We completed a Phase 2 trial of PRX-03140 alone and in combination with an approved drug for Alzheimer's disease (the cholinesterase inhibitor Aricept (donepezil)) in patients with Alzheimer's disease in the fourth quarter of 2007. This randomized, double-blind, placebo-controlled, multiple ascending dose trial enrolled 80 patients with mild Alzheimer's disease. Patients were studied on PRX-03140 across three dose groups of 10 patients each: 50 mg once-daily, 150 mg once-daily and placebo, or in a placebo-controlled combination across five dose arms of 10 patients each: PRX-03140 at 5, 25, 50, 100 and 200 mg with Aricept 10 mg once-daily.

The two primary endpoints of the trial were: (1) to assess the safety and tolerability of PRX-03140 in patients with Alzheimer's disease when dosed orally once-daily for 14 days alone and in combination with donepezil, and (2) to assess the effect of PRX-03140 on brain wave activity, as was performed in the Phase 1b clinical trial. Secondary endpoints of the trial included evaluating the pharmacokinetic effect of PRX-03140 on Aricept concentrations in patients with mild Alzheimer's disease and assessing the effects of repeat doses of PRX-03140 on a battery of standardized cognitive function tests, such as the Alzheimer's Disease Assessment Scale cognitive subscale (ADAS-cog). ADAS-cog is the current standard for evaluating drug efficacy for cognition in Alzheimer's disease and is an established and accepted FDA registration endpoint.

Efficacy results showed that patients receiving 150 mg of PRX-03140 orally once daily as monotherapy achieved a mean 3.6 point improvement on the ADAS-cog versus a 0.9 point worsening in patients on placebo. This result corresponds to a p-value of 0.021, which is statistically significant. Data for the patients on a 50 mg dose of PRX-03140 showed a 1.0 point improvement on the ADAS-cog. The monotherapy dose response (150 mg versus 50 mg versus placebo) was also statistically significant (p=0.026). ADAS-cog changes in the combination arms of the trial were not statistically significant.

This trial also used Mindstreams, an automated battery of computerized cognitive function tests, as a secondary endpoint. Patients on PRX-03140 monotherapy demonstrated statistically significant (p<0.04)



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improvements in memory and visual-spatial indices as measured using Mindstreams when compared with placebo. PRX-03140 also produced positive trends in the alteration in brain wave activity in the 150 mg dose group versus placebo, similar to the changes observed with currently approved drugs for Alzheimer's disease.

PRX-03140 appeared to be well tolerated in this trial, both alone and in combination with Aricept. No serious drug-related adverse events occurred during the trial.

In May 2008, we initiated two Phase 2b trials in Alzheimer's disease. The first trial investigates PRX-03140 in combination with 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 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.

The second trial initiated in May 2008 investigates 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; 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 also includes a three-month optional extension.

Pursuant to a development and license agreement entered into on December 11, 2006, we granted GlaxoSmithKline an option to obtain exclusive, worldwide license rights to complete the development of, and commercialize, PRX-03140. For a description of the collaboration agreement with GlaxoSmithKline, see Business Strategic Alliances And Collaborations below.

### *PRX-08066 for Pulmonary Hypertension*

PRX-08066 is a novel, highly selective, small-molecule inhibitor, or antagonist, of a specific GPCR known as 5-HT<sub>2B</sub>. We are developing PRX-08066 for the treatment of pulmonary hypertension associated with COPD. Pulmonary hypertension, or PH, in general is a serious, often fatal cardiovascular disease characterized by elevation of pulmonary blood pressure and progressive thickening and narrowing of the blood vessels of the lungs, often leading to heart failure.

We completed a Phase 2 trial of PRX-08066 in PH associated with 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.

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We have completed three Phase 1 clinical trials of PRX-08066 in healthy volunteers, including a Phase 1b clinical trial in athletes conditioned to exercise at high altitudes. Results from the Phase 1b trial showed that, compared with placebo, PRX-08066 caused a statistically significant reduction in the increase in systolic pulmonary blood pressure observed during exercise in volunteers breathing low oxygen. In the two earlier Phase 1 trials as well as the Phase 1b trial, PRX-08066 was well-tolerated, with a half-life of approximately 16 hours, supporting once daily oral dosing. To date, there have been no serious adverse events associated with treatment with PRX-08066.

In August 2008, we initiated a Phase 2b right-heart catheter study of PRX-08066 in patients with COPD and moderate-to-severe PH. This 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. The trial is designed to enroll adult patients with COPD and moderate-to-severe PH.

### *PRX-07034 for Cognitive Impairment associated with Schizophrenia*

PRX-07034 is a novel, highly selective, small-molecule antagonist of a specific GPCR known as 5-HT<sub>6</sub>. We have completed multiple Phase 1 studies of PRX-07034 and, prior to October 2008, we were developing PRX-07034 for the treatment of cognitive impairment associated with schizophrenia. We have suspended further development of this program as part of a cost reduction initiative implemented in October 2008. Future development of this program is dependent upon our ability to raise a significant amount of additional capital.

## **VASOVIST**

Vasovist is an internally discovered, injectable intravascular contrast agent that is designed to provide improved imaging of the vascular system using magnetic resonance angiography, or MRA. On December 22, 2008, the FDA approved Vasovist for marketing to evaluate aortoiliac occlusive disease (AIOD) in adults with known or suspected peripheral vascular disease. AIOD occurs when iliac arteries become narrowed or blocked, which may prevent the sufficient transport of oxygen and/or blood throughout the body. Vasovist is the first contrast agent approved for marketing in the United States for use with MRA, a non-invasive modality for imaging blood vessels. Vasovist has also been approved for marketing in more than 30 countries outside of the United States.

Vasovist reversibly binds to the human blood protein albumin, allowing imaging of the blood vessels for approximately an hour after administration. With a single injection, Vasovist enables the capture of three-dimensional images of arteries and veins in the body. Vasovist may make it possible for physicians to detect vascular disease earlier, more safely and less invasively than with X-ray angiography, and for physicians to provide an improved evaluation of potential therapeutic options including percutaneous intervention and vascular surgery.

In September 2008, our development and commercialization partner for Vasovist, Bayer Schering, terminated the Amended and Restated Strategic Collaboration Agreement by and between us and Bayer Schering, dated as of June 9, 2000 and amended as of December 22, 2000, effective March 1, 2009. Accordingly, the worldwide commercial rights for Vasovist were transferred back to us on such date. It is our intention to sell the commercial rights to Vasovist, however there is no guarantee that we will be able to do so. In addition, upon a sale of the commercial rights to Vasovist, we will be required to reimburse Bayer Schering for a portion of their development costs. The reimbursement will be based on pre-defined percentages of the development costs, allocated to each territory for which the commercial rights are sold, with full worldwide rights amounting to a \$33 million reimbursement to Bayer Schering.

## **OUR THERAPEUTIC DRUG DISCOVERY TECHNOLOGY AND APPROACH**

We have developed a novel and proprietary in silico protein structure-based approach to GPCR and ion channel-targeted drug discovery that allows us to benefit from the structure-based approach in the absence of

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experimentally-determined structures for these targets. Our PREDICT technology combines genomic information (the amino acid sequence of the target protein) with physical and chemical properties of the cell membrane environment to determine the most stable 3D structure of a membrane-bound protein. The use of our PREDICT technology to determine a 3D structure of the target protein is the foundation and first step in our novel system of discovery and optimization for GPCR and ion channel-targeted drugs. We maintain our GPCR and ion channel structures as trade secrets, which, when combined with our proprietary software and the know-how required to use the PREDICT technology, we believe creates a strong barrier to entry for our competitors.

Using our proprietary drug discovery technology and approach requires the successive application of the following five steps: (1) using our PREDICT technology to identify the most stable 3D structure of the desired GPCR or ion channel drug target, bypassing the need for X-ray crystallography, (2) analyzing the resulting 3D structure and identifying a potential binding site on the target structure for drug interaction, (3) performing in silico screening using the computer to virtually fit more than four million drug-like compounds into this drug site, ensuring that both the shape and chemical properties of the binding site and the compound match, (4) selecting the approximately 100-200 compounds that best match the binding site on the target and testing their activity in vitro in the laboratory and (5) identifying the most active and novel chemical compounds, referred to as lead compounds, and then subjecting these lead compounds to an integrated structure-based lead optimization process. The PREDICT-generated 3D structure of the target protein as well as other 3D protein structures (many of which are also generated by PREDICT) and more traditional medicinal chemistry efforts are used to steer lead optimization along the most efficient path, transforming lead compounds into drug candidates expeditiously. Our discovery and optimization process is outlined in the following steps:

*PREDICT-3D in silico modeling.* We have developed novel proprietary algorithms which we use in our PREDICT technology to model the 3D structure of targets of interest (GPCRs and ion channel proteins) from their primary amino acid sequence. PREDICT uses algorithms that explore a large number of possible structures of the target and then selects the biologically relevant one. It takes into account specific interactions between the target protein and the membrane, specific interactions within the target protein itself, and addresses the limitations that hamper homology-based modeling of GPCRs and ion channel proteins. The PREDICT software code and many of its algorithms are kept as trade secrets, making it difficult to copy or reverse engineer. We filed patent applications for PREDICT version 1.0 in 2000. The current version of PREDICT has evolved considerably from the original version and includes numerous new algorithms and capabilities. PREDICT bypasses the need for X-ray crystallography structures of the GPCR or ion channel protein target to initiate a structure-based (so-called rational) drug discovery program.

*Virtual libraries.* Our libraries consist of in silico versions of four million drug-like compounds which are available for purchase from commercial vendors worldwide. These virtual libraries reduce the need for us to synthesize or purchase, store and maintain tens or hundreds of thousands of actual compounds for the initial screening.

*Rapid in silico screening.* The process of in silico screening requires the computer to perform trillions of operations in trying to fit numerous drug-like compounds into the binding site of the target protein, matching both shape and chemical properties. We perform high-throughput in silico screening with a combination of proprietary and commercially available public software to identify compounds that may bind to a target GPCR or ion channel protein.

*Ranking of screening results.* We have developed proprietary algorithms for ranking our in silico screening results using internally developed tools, which we believe enables us to select the 100-200 most promising compounds for in vitro testing.

*Integrated structure-based lead optimization.* The most promising novel lead compounds, identified in silico and shown to have binding affinity and functionality in vitro, are optimized into drug candidates using an integrated structure-based approach. This process makes use of the PREDICT 3D structures (of the drug target and related off-target proteins) as well as many other in silico tools that we have created or acquired to enable efficient structure-based lead optimization, leading to highly selective

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drug candidates. These tools allow us to overcome challenges frequently encountered during lead optimization, such as selectivity, blood-brain barrier penetration and hERG ion channel binding, in a fraction of the time and cost compared to traditional lead optimization efforts. Using these in silico tools, our computational and medicinal chemists are able to select for actual synthesis the most promising subset of suggested compounds for further optimization. In each of our clinical-stage programs, this approach has allowed us to synthesize fewer than 10% of the compounds that we believe would have been synthesized if we were to follow the traditional methods of lead optimization.

## **STRATEGIC ALLIANCES AND COLLABORATIONS**

### ***GlaxoSmithKline***

On December 11, 2006, we entered into a development and license agreement with SmithKline Beecham Corporation, doing business as GlaxoSmithKline, and Glaxo Group Limited to develop and commercialize medicines targeting four GPCRs, for the treatment of a variety of diseases, including an option to license our 5-HT<sub>4</sub> partial agonist, PRX-03140. The other three GPCR targets identified under the collaboration are early discovery programs. GlaxoSmithKline does not have options to any of our other clinical programs besides PRX-03140. Our collaboration with GlaxoSmithKline is being conducted through its Center of Excellence for External Drug Discovery.

Under the terms of the agreement, we are obligated to carry out a research and development program for PRX-03140 and three research targets, and to discover and develop compound candidates through proof of concept, typically defined as the completion of Phase 2 clinical studies. Upon completion of the proof of concept package for each of the four programs, GlaxoSmithKline has the exclusive option, exercisable at GlaxoSmithKline's sole discretion, to obtain exclusive, worldwide license rights to complete the development and to commercialize products based on such compound. The research term, which began on December 11, 2006, continues for a minimum of six years and may be extended to December 11, 2020. During the research term, we are obligated to participate on a joint steering committee, comprised of members from GlaxoSmithKline and us, that oversees the collaboration. At the end of the research term, we can elect at any time to withdraw from participation in the joint steering committee or other committees established under the agreement. We have retained an option to co-promote products successfully developed from the PRX-03140 program in the United States. Under any such co-promotion arrangement, the collaboration agreement provides for GlaxoSmithKline to direct the promotional strategy and compensate us for our efforts in co-promoting the product. In connection with a workforce reduction that we implemented in March 2009, we entered into a letter agreement with GlaxoSmithKline allowing us to reduce our research and development obligations under our development and license agreement, during the period from March 13, 2009 to September 13, 2009, for programs other than the PRX-03140 program.

In return for the exclusive options described above, and in consideration of the development work to be performed by us under the collaboration agreement, GlaxoSmithKline paid us an initial payment of \$17.5 million. Additionally, as part of the collaboration, on December 11, 2006, we entered into a stock purchase agreement with GlaxoSmithKline providing for the issuance and sale to GlaxoSmithKline of 3,009,027 shares of our common stock for an aggregate purchase price of \$17.5 million. In addition, we may be eligible for up to an aggregate of \$1.2 billion in additional nonrefundable option fees and milestone payments relating to the achievement of certain development, regulatory and commercial milestones across the four research programs. To date, we have received an aggregate of \$19 million in such milestone payments related to the initiation of the Phase 2b studies for PRX-03140 and the identification of a total of nine lead candidates, three from each of the discovery programs, to move forward into lead optimization. We are also eligible to receive tiered, double-digit royalties based on net sales by GlaxoSmithKline of any products developed under the collaboration agreement. The specific royalty rates will vary depending upon a number of factors, including the total annual net sales of the product and whether it is covered by one of our patents. GlaxoSmithKline's royalty obligation under the collaboration agreement generally terminates on a product-by-product and

country-by-country basis upon the later of (i) the expiration of our last patent claiming the manufacture, use, sale or importation of the product in the relevant country and (ii) twelve years after the first commercial sale of the product in the relevant country. GlaxoSmithKline accounted for 76% and 53% of our revenue in the years



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ended December 31, 2008 and 2007, respectively. Although we are eligible for milestone payments, option fees and royalty payments under the collaboration agreement, we do not expect any such payments will extend our available cash beyond the end of August 2009.

If GlaxoSmithKline does not exercise any of the four options, the collaboration agreement will expire upon the expiration of the last such option. Otherwise, the collaboration agreement will expire on a product-by-product and country-by-country basis upon the expiration of the royalty payment obligations for each product in each country.

We have responsibility and control for filing, prosecution or maintenance of any of our patents that are the subject of an option to GlaxoSmithKline under the collaboration agreement, provided that in the event an option is exercised, responsibility and control of the patents subject to such option transfers to GlaxoSmithKline.

The parties each have the right to terminate the collaboration agreement if the other party becomes insolvent or commits an uncured material breach of the collaboration agreement. In addition, GlaxoSmithKline has the right to terminate the collaboration agreement in its entirety, and to terminate its rights to any program developed under the collaboration agreement on a regional or worldwide basis, in each case without cause. Upon a termination of the collaboration agreement, depending upon the circumstances, the parties have varying rights and obligations with respect to the grant of continuing license rights, continued commercialization rights and continuing royalty obligations.

***Amgen***

On July 31, 2006, we entered into an exclusive license agreement with Amgen Inc. to develop and commercialize 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. The S1P1 receptor is a cell surface GPCR found on white blood cells and in other tissues that is associated with certain autoimmune diseases, such as rheumatoid arthritis and multiple sclerosis.

Pursuant to the license agreement, we granted Amgen an exclusive worldwide license to our intellectual property and know-how related to the compounds in our S1P1 program that modulate the S1P1 receptor, for the development and commercialization of those compounds and other compounds and products that modulate the S1P1 receptor. Amgen has limited rights to sublicense its rights under the license. In return for the license, Amgen paid us a nonrefundable, up-front payment of \$20 million and is obligated to pay us royalties based on aggregate annual net sales of all S1P1-receptor-modulating products developed by Amgen under the license agreement. In addition, we may be eligible for up to an aggregate of \$287.5 million of nonrefundable milestone payments that relate to milestones associated with the commencement of clinical trials, regulatory approvals and annual net sales thresholds of the products under the license agreement. These royalty rates and milestone amounts are subject to reduction in the event that, among other things:

Amgen is required to obtain third-party rights to develop and commercialize a product that incorporates an EPIX compound; and

Amgen develops and commercializes products that are not covered by the intellectual property rights we licensed to Amgen, such as for example, S1P1-modulating products that may be acquired by Amgen from a third-party.

Although we are eligible for milestone payments and royalty payments under the agreement, we do not expect any such payments will extend our available cash beyond the end of August 2009.

Generally, Amgen's royalty obligation under the agreement terminates on a product-by-product and country-by-country basis upon the later of (a) the expiration or termination of the last claim within the patents (whether such patents are patents EPIX licensed to Amgen or are patents owned or in-licensed by Amgen) covering such product and (b) ten years following the first commercial sale of the product. The agreement expires when all of Amgen's royalty obligations have terminated.

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We have the option to co-promote one product from the collaboration in the United States for one indication to be jointly selected by EPIX and Amgen. During the first 15 months of the agreement, we were required to design, discover and develop, at our own cost, additional compounds that modulate the S1P1 receptor and that are within the same family of compounds as those identified in our patent applications licensed to Amgen under the agreement. The collaboration agreement provides Amgen with a license to these additional compounds to further its development efforts. We may undertake additional research under the agreement, at our own expense, as approved by a joint steering committee formed pursuant to the agreement. We had responsibility and control for filing, prosecution or maintenance for any of our patents licensed to Amgen for 24 months, at which time, responsibility and control of such patents transferred to Amgen. Amgen now has responsibility and control for filing, prosecution or maintenance for all patents covered by the agreement, including patents jointly developed under the agreement. Amgen will have final decision making authority on all other research matters and will be responsible for non-clinical and clinical development, manufacturing, regulatory activities and commercialization of the compounds and products developed under the license agreement, at its own expense.

The parties each have the right to terminate the agreement (in whole or for specified products or countries, depending upon the circumstances) upon a material uncured breach by the other party and Amgen has the right to terminate the agreement for convenience upon varying periods of at least three months advance notice. Upon a termination of the agreement, depending upon the circumstances, the parties have varying rights and obligations with respect to the grant of continuing license rights, continued commercialization rights and continuing royalty obligations.

### ***Cystic Fibrosis Foundation Therapeutics, Incorporated***

On April 1, 2008, we entered into a new research, development and commercialization agreement with Cystic Fibrosis Foundation Therapeutics, Incorporated, or CFFT, the drug discovery and development affiliate of the Cystic Fibrosis Foundation. The agreement provides for the continuation of the first research program initiated under a prior research, development and commercialization agreement between us and CFFT dated March 7, 2005, as amended. Under the April 2008 agreement, we have agreed to conduct additional research activities aimed at developing a compound to correct a malfunction of the cystic fibrosis transmembrane conductance regulator protein. CFFT may make payments of up to \$30.7 million under the agreement for research services and reimbursed research costs. We may also be eligible to receive up to an additional \$7.0 million for the achievement of certain development milestones. We do not currently expect that any payments for which we may be eligible from CFFT will materially supplement our cash position prior to the end of August 2009, if at all.

Upon any commercialization by us of a product developed under the agreement, we are required to pay tiered royalties to CFFT based on net sales by us of such product. In addition, we are required to make certain payments to CFFT if we outlicense a product developed under the agreement.

The research program is scheduled to conclude on April 1, 2017, but can be extended for up to three additional years if we are conducting a certain clinical trial, or by agreement of the parties. The agreement terminates at such time when there are no longer any royalty payment obligations owing under the agreement. Upon an earlier termination of the agreement by either party, depending upon the circumstances, the parties have varying rights and obligations with respect to intellectual property rights and payment obligations. CFFT accounted for 17% and 25% of our revenue in the years ended December 31, 2008 and 2007, respectively.

### ***Bayer Schering***

In September 2008, Bayer Schering Pharma AG, Germany, terminated the Amended and Restated Strategic Collaboration Agreement by and between us and Bayer Schering, dated as of June 9, 2000 and amended as of December 22, 2000, effective March 1, 2009. Accordingly, the worldwide commercial rights for our blood pool

magnetic resonance angiography agent, Vasovist, were transferred back to us on such date.

Under the agreement, we granted Bayer Schering an exclusive license to co-develop and market Vasovist worldwide. Generally, each party to the agreement shared equally in the costs to develop Vasovist. Pursuant to

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the terms of the Agreement, we retained responsibility for completing clinical trials and filing for FDA approval in the United States, and Bayer Schering retained responsibility for clinical and regulatory activities for Vasovist outside the United States. In addition, we were entitled to receive a royalty on products sold outside the United States and a percentage of Bayer Schering's operating profit margin on products sold in the United States. In connection with this strategic collaboration and the amendment to our strategic collaboration agreement with Covidien in 2000, as described under Intellectual Property below, Bayer Schering paid us an up-front fee of \$10 million, which we then paid to Covidien. Under the agreement, Bayer Schering also paid us \$20 million in exchange for shares of our common stock.

Bayer Schering had the right to terminate the agreement at any time on a region-by-region basis or in its entirety, upon six months written notice to us, which right was exercised as described above. In addition, either party had the right to terminate the agreement while still in effect upon thirty days notice if there is a material breach. Upon termination of the agreement, all patent rights granted to Bayer Schering terminated and Bayer Schering was required to grant us an exclusive, worldwide royalty bearing license for any related patent rights owned by Bayer Schering. In addition, if we subsequently enter into an agreement with a third party for the commercialization of Vasovist, which is our current intention, we will be required under the agreement to reimburse Bayer Schering for a portion of their development costs. The reimbursement will be based on pre-defined percentages of the development costs, allocated to each territory for which the commercial rights are sold, with full worldwide rights amounting to a \$33 million reimbursement to Bayer Schering.

## **TECHNOLOGY AGREEMENTS**

### ***Covidien***

In August 1996, we entered into a strategic collaboration agreement with Mallinckrodt Inc. (subsequently acquired by Covidien Ltd.), involving research, development and marketing of MRI vascular contrast agents developed or in-licensed by either party. In June 2000, in connection with the exclusive license that we granted to Bayer Schering under our strategic collaboration agreement, we amended our strategic collaboration with Covidien. The amendment enabled us to sublicense certain technology from Covidien to Bayer Schering which allowed us to enter into the strategic collaboration agreement for Vasovist with Bayer Schering. Pursuant to that amendment, we also granted to Covidien a non-exclusive, worldwide license to manufacture Vasovist for clinical development and commercial use on behalf of Bayer Schering in accordance with a manufacturing agreement entered into in June 2000 between Covidien and Bayer Schering. In connection with this amendment, we paid Covidien an up-front fee of \$10.0 million and were obligated to pay up to an additional \$5.0 million in milestone payments, of which \$2.5 million was paid following the NDA filing in February 2004 and \$2.5 million was recognized as a royalty expense upon marketing approval in the United States by the FDA in December 2008 and was paid to Covidien in January 2009. We are also required to pay Covidien a share of our Vasovist operating profit margins in the United States and a percentage of any royalty we receive on Vasovist gross profits outside the United States.

As a result of the termination of our strategic collaboration agreement with Bayer Schering effective March 1, 2009, Bayer Schering is required to assign to us certain rights and obligations under the June 2000 manufacturing agreement between Bayer Schering and Covidien. We are currently in discussions with Covidien regarding such assignment. Covidien is currently the only manufacturer approved by the FDA to produce Vasovist.

## **COMPETITION**

We face, and will continue to face, intense competition from pharmaceutical and biotechnology companies, as well as numerous academic and research institutions and governmental agencies engaged in drug discovery activities or funding, both in the United States and abroad. Some of these competitors are pursuing the development of product

candidates that target the same indications that we are targeting for our clinical and preclinical programs. Even if we and our collaborators are successful in developing our clinical-stage candidates, the resulting products will compete with a variety of established products.

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Significant competitors in the area of GPCR-focused drug discovery include Arena Pharmaceuticals, Acadia Pharmaceuticals, Addex Pharmaceuticals and 7TM Pharma, and for ion channels our competitors include Vertex Pharmaceuticals and Sucampo Pharmaceuticals. In addition, most large pharmaceutical companies have drug discovery programs that target GPCRs and ion channels.

Many of our competitors have significantly greater financial, manufacturing, marketing and product development experience and resources than we do. These companies also have significantly greater research and development capabilities than we do, and have significantly greater experience than we do in preclinical and clinical trials of potential pharmaceutical products, and in obtaining FDA and other regulatory clearances. Our commercial opportunity will be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer side effects or are less expensive than any products that we may develop.

If our clinical-stage drug candidates are approved, they will compete with currently approved drugs and potentially with drug candidates currently in development for the same indications, 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 Medivation, Inc., GlaxoSmithKline plc and Pfizer, Inc. We are studying PRX-03140 both as monotherapy and in combination with approved products such as Aricept, which is marketed by Pfizer Inc.

*PRX-08066.* If approved, PRX-08066, the drug candidate we are developing for the treatment of pulmonary hypertension associated with COPD, 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 Bayer Schering Pharma AG.

*PRX-07034.* If approved for the treatment of cognitive impairment (associated with schizophrenia), 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.

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, or MRA, 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 Imaging S.P.A. and OptiMARK by Covidien Ltd. We also are aware of certain agents under clinical development that have been or are being evaluated for use in MRA: 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. In addition to competition within the MRI field, we also face competition from other imaging technologies, including CT scans, ultrasounds, and X-ray scans.

## **INTELLECTUAL PROPERTY**

We actively seek to protect the proprietary technology that we consider important to our business, including chemical species, compositions and formulations, their methods of use and processes for their manufacture, as new intellectual property is developed. In addition to seeking patent protection in the United States, we plan to selectively file patent

applications in certain additional foreign countries in order to further protect the inventions that we consider important to the development of our foreign business. We also rely upon trade secrets and contracts to protect our proprietary information.

As of February 2009, our patent portfolio included a total of 18 issued U.S. patents, 129 issued foreign patents and 275 pending patent applications in the United States and other countries with claims covering the composition of matter and methods of use for all of our preclinical and clinical-stage candidates and Vasovist.



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In addition to patents, we rely where necessary upon unpatented trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our collaborators, employees and consultants and invention assignment agreements with our employees. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

In addition, we license, and expect to continue to license, third-party technologies and other intellectual property rights that are incorporated into some elements of our drug discovery and development efforts. Set forth below are our significant license agreements.

### ***Ramot***

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. Pursuant to this license, we have exclusive, worldwide rights to certain technology developed at Tel Aviv University to develop, commercialize and sell products for the treatment of diseases or conditions in humans and animals. The licensed technology, as continually modified, added to and enhanced by us, consists in large part of computer-based models of biological receptors and methods of designing drugs to bind to those receptors.

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, and we would be required to make payments to Ramot, as described below, if and when rights to any such drug candidates are ever sublicensed or any such drug candidates are commercialized. In addition, we have used the licensed technology in all of our preclinical-stage programs and would expect to make payments to Ramot if rights to any drug candidates were ever commercialized from any of these programs. One of our employees, Sharon Shacham, Senior Vice President of Drug Development, was one of the inventors of the technology that we license from Ramot. We believe that Ramot shares a portion of any royalty income received with the respective inventors and, accordingly, Dr. Shacham receives a portion of the amounts we pay Ramot.

We paid Ramot an upfront fee of \$40,000 upon the grant of the license. Under the license, we have an obligation to make royalty payments to Ramot on our net sales of products that are identified, characterized or developed through the use of the licensed technology that are either 1.5% or 2.5% of such net sales (depending upon the degree to which the product needed to be modified after being identified, characterized or developed through the use of the licensed technology) and decrease as the volume of sales increases. The royalty obligation for each product expires on a country-by-country basis twelve years after the first commercial sale. There is also an annual minimum royalty payment obligation of \$10,000 per year.

We also are required to share between 5% and 10% of the consideration we receive from parties to whom we grant sublicenses of rights in the Ramot technology or sublicenses of rights in products identified, characterized or developed with the use of such technology and between 2% and 4% of consideration we receive from performing services using such technology. In connection with our collaborations with GlaxoSmithKline, Amgen and CFFT, we have to date paid \$3.3 million in total royalties to Ramot primarily for amounts received to date for the upfront payments and milestone payments received under these license agreements.

The license may be terminated by either party upon a material breach by the other party unless cured within 30 days, in the case of a payment breach, and 90 days in the case of any other breach. The license may also be terminated by either party in connection with the bankruptcy or insolvency of the other party. The license expires upon the

expiration of our obligation to make payments to Ramot. Therefore, since we have an ongoing obligation to pay annual minimum royalties to Ramot as described above, the license may not expire and may only terminate upon a breach by, or bankruptcy of, a party.

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### ***Massachusetts General Hospital***

In July 1995, we entered into a license agreement with Massachusetts General Hospital, or MGH, pursuant to which MGH granted us an exclusive worldwide license to patents and patent applications which relate to Vasovist. The MGH license requires us to pay royalties on the net sales of products covered by this license, including Primovist, MultiHance and Vasovist. We have paid MGH approximately \$0.7 million in royalty payments through 2008 under this license agreement. The license agreement expires on a country-by-country basis when the patents covered by the license agreement expire, the majority of which expired in November 2006. The license agreement does not contain a renewal provision. We believe that the expiration of these patents does not compromise our proprietary position with respect to Vasovist because Vasovist is covered by composition of matter patents independent of our license with MGH. These composition of matter patents extend into 2015 in the United States, although the life of these patents may be extended.

### ***Prince***

In November 2003, we entered into an intellectual property agreement with Martin R. Prince, M.D., Ph.D., an early innovator in the field of MRA relating to dynamic MRA, which involves capturing MRA images during the limited time, typically 30 to 60 seconds, available for imaging with extracellular agents. 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. In consideration of Dr. Prince entering into the agreement, we agreed to pay him an upfront fee of \$850,000 and royalties on sales of Vasovist consistent with a non-exclusive early stage academic license and delivered to him 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 per year during the term of the agreement. The agreement expires upon the expiration of the last patent under the agreement. The agreement is subject to termination by either party upon the incurred material breach of the agreement by the other party.

## **MARKETING, SALES AND DISTRIBUTION**

We currently have no marketing, sales or distribution capabilities. To commercialize any of our drug candidates we must develop these capabilities internally or through collaboration with third-parties. In selected indications where we believe that our products can be commercialized by a specialty sales force that calls on a limited but focused group of physicians, we may commercialize our products in the United States. For example, we believe that pulmonary specialists who treat pulmonary hypertension, and the centers in which they practice, are sufficiently concentrated to enable us to effectively promote PRX-08066, if approved by the FDA, to this market in the United States with a small internal sales force. In therapeutic or diagnostic areas that require a large sales force selling to a large and diverse prescribing population and for markets outside of the United States, we plan to establish collaborations with pharmaceutical or biotechnology companies for commercialization of our drug candidates. With respect to Vasovist, in September, 2008, Bayer Schering terminated the strategic collaboration agreement between us and Bayer Schering relating to Vasovist, effective March 1, 2009. Accordingly, the worldwide commercial rights for Vasovist were transferred back to us on such date. It is our intention to sell the commercial rights to Vasovist. However, there is no guarantee that we will be able to do so. With respect to PRX-03140, we have granted GlaxoSmithKline an exclusive option to obtain exclusive, worldwide license rights to complete the development and commercialization of PRX-03140. With respect to our preclinical compounds that modulate the S1P1 receptor, we have granted Amgen an exclusive worldwide license for the development and commercialization of those compounds.

## **MANUFACTURING**

We outsource and plan to continue to outsource manufacturing responsibilities to third-parties for our existing and future therapeutic drug candidates for clinical development and commercial purposes. If one of our manufacturers for our therapeutic product candidates should become unavailable to us for any reason, we

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believe that there are a number of potential replacements as our processes are not manufacturer-specific, though we may incur some added cost and delay in identifying or qualifying such replacements, including delays associated with the need for FDA review and approval of the new manufacturer, as well as those associated with the new manufacturer's ability to establish the manufacturing process.

We do not have the capability to manufacture Vasovist. As a result of the termination of our strategic collaboration agreement with Bayer Schering effective March 1, 2009, Bayer Schering is required to assign to us certain rights and obligations under the June 2000 manufacturing agreement between Bayer Schering and Covidien. If we were to sell the commercial rights to Vasovist, the buying party would be responsible for establishing a manufacturing source for Vasovist. Covidien is currently the only manufacturer approved by the FDA to produce 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. Our agreements with these suppliers generally operate on a work order basis, with no minimum purchase requirements and are generally terminable by us upon 60 days and 90 days prior written notice, respectively. Small amounts of material used for preclinical research and development purposes are synthesized in-house or with third-party contract laboratories. The production of our small molecule drug candidates PRX-03140, PRX-08066 and PRX-07034 use synthetic organic chemistry procedures that are standard in the pharmaceutical industry. There are no complicated chemistries or unusual equipment required in the manufacturing process of these drug candidates. PRX-03140, PRX-08066 and PRX-07034 are all currently administered as unformulated drug products. A commercially viable formulation will need to be developed, manufactured and certified for each of these drug candidates. The final commercial formulation may not prove to be bioequivalent to the current formulation. This may result in the need to initiate additional clinical trials to define new dosing regimes. Furthermore, the development and implementation of a new formulation and commercial process for cGMP manufacturing may add significant delays to additional clinical trials, regulatory filings and commercial launch.

## **GOVERNMENT REGULATION AND PRODUCT APPROVAL**

The FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries impose substantial requirements upon the clinical development, manufacture and marketing of pharmaceutical products. These agencies and other federal, state and local entities regulate, among other things, the testing, manufacture, quality control, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, advertising and promotion of our products. Failure to comply with regulatory requirements may result in criminal prosecution, civil penalties, recall or seizure of products, total or partial suspension of production or injunction, as well as other actions that could affect our product candidates or us. Any failure to comply with regulatory requirements, to obtain and maintain regulatory approvals, or any delay in obtaining regulatory approvals could materially adversely affect our business.

The process required by the FDA before drugs may be marketed in the United States generally involves the following:

- preclinical laboratory and animal studies;

- submission of an investigational new drug application, or IND, which must become effective before human clinical trials may begin;

- adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug for its intended use; and

- FDA approval of a new drug application, or NDA.

The testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for any of our drug candidates will be granted on a timely basis, if at all.

Once a pharmaceutical candidate is identified for development it enters the preclinical testing stage. During preclinical studies, laboratory and animal studies are conducted to show biological activity of the drug

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candidate in animals, both healthy and with the targeted disease. Also, preclinical tests evaluate the safety of drug candidates. Preclinical tests must be conducted in compliance with good laboratory practice regulations. In some cases, long-term preclinical studies are conducted while clinical studies are ongoing.

Prior to commencing a clinical trial, we must submit an IND to the FDA. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the trial. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Our submission of an IND may not result in FDA authorization to commence a clinical trial. All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with good clinical practice regulations. These regulations include the requirement that all subjects provide informed consent. Further, an institutional review board, or IRB, at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution. Progress reports providing updated information on the clinical trials, including the results, if available, must be submitted at least annually to the FDA and more frequently if adverse events or other certain types of changes occur.

Human clinical trials are typically conducted in three sequential phases that may overlap:

*Phase 1:* The drug is initially introduced into healthy human subjects or patients with the disease and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion.

*Phase 2:* Involves studies in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

*Phase 3:* Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. These studies are intended to establish the overall risk-benefit ratio of the product and provide an adequate basis for product labeling.

In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients. Because these patients already have the target disease, these studies may provide initial evidence of efficacy traditionally obtained in Phase 2 clinical trials, and thus these trials are frequently referred to by industry as Phase 1/2 clinical trials.

The FDA or an IRB or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

Concurrent with clinical trials and preclinical studies, companies also must develop information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and the manufacturer must develop methods for testing the quality, purity and potency of the final drugs. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf-life.

A sponsor of an IND may request that the FDA evaluate within 45 days certain protocols and issues relating to the protocols. Such Special Protocol Assessments, or SPAs, may be requested for clinical protocols for Phase 3 clinical trials whose data will form the primary basis for an efficacy claim if the trials had been the subject of discussion at an end-of-Phase 2 / pre-Phase 3 meeting. If the sponsor and the FDA reach a written agreement regarding the protocol, the SPA will be considered binding on the FDA and will not be changed unless the sponsor fails to follow the

agreed-upon protocol, data supporting the request are found to be false or incomplete, or the FDA determines that a substantial scientific issue essential to determining the safety or effectiveness of the drug was identified after the testing began. Even if a SPA is agreed to, approval of the NDA is not guaranteed since a final determination that an agreed-upon protocol satisfies a specific



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objective, such as the demonstration of efficacy, or supports an approval decision, will be based on a complete review of all the data in the NDA.

The results of product development, preclinical studies and clinical studies, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, results of chemical studies and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The FDA reviews all NDAs submitted before it accepts them for filing. It may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. The submission of an NDA is subject to the payment of substantial user fees, but a waiver of such fees may be obtained under certain circumstances. The FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data. Even if such data is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. In addition, the FDA may require testing and surveillance programs to monitor the use or longer term effects of approved products that have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs.

The FDA has various programs, including fast track, priority review and accelerated approval that are intended to expedite or simplify the process for reviewing drugs and/or provide for approval on the basis of surrogate endpoints. Generally, drugs that may be eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs, and those that offer meaningful benefits over existing treatments. For example, priority review applies to new drugs that have the potential for providing significant improvements compared to marketed products in the treatment or prevention of a disease. Although priority review does not affect the standards for approval, FDA will attempt to expedite review of the application for a drug designated for priority review. We do not know whether our drugs will be eligible for, or whether we will apply for, any of these programs. Even if a drug qualifies for one or more of these programs, we cannot be sure that the time period for FDA review will be shortened.

Satisfaction of FDA requirements or similar requirements of state, local and foreign regulatory agencies typically takes at least several years and the actual time required may vary substantially, based upon, among other things, the type, complexity and novelty of the product or disease. Government regulation may delay or prevent marketing of potential products for a considerable period of time and impose costly procedures upon our activities. Success in early-stage clinical trials does not assure success in later-stage clinical trials. Data obtained from clinical activities are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. Even if a product receives regulatory approval, the approval may be significantly limited to specific diseases, conditions, patient populations and dosages. Further, even after regulatory approval is obtained, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. Delays in obtaining, or failures to obtain regulatory approvals for any drug candidate could substantially harm our business and cause our stock price to drop significantly. In addition, we cannot predict what adverse governmental regulations may arise from future U.S. or foreign governmental action.

Any drug products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the drug, drug sampling and distribution requirements, notifying the FDA and gaining its approval of certain changes to the product, including manufacturing and labeling changes, complying with certain electronic records and signature requirements and complying with FDA promotion and advertising requirements. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with regulatory requirement

including cGMP, which apply to all stages and aspects of the manufacturing process and impose considerable procedural and documentation requirements

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upon us and our contract manufacturers. We cannot be certain that we or our present or future suppliers will be able to comply with the pharmaceutical cGMP regulations and other FDA regulatory requirements.

The FDA's policies may change and additional government regulations may be enacted which could prevent or delay regulatory approval of our drug candidates or significantly change the statutory and regulatory provisions relating to the manufacturing, marketing and postmarket surveillance of drug products. For example, the Food and Drug Administration Amendments Act of 2007, or the FDAAA, was enacted in September 2007, giving the FDA enhanced postmarket authorities, such as the authority to require postmarket studies and clinical trials, labeling changes based on new safety information, and compliance with a risk evaluation and mitigation strategy approved by the FDA. FDA's postmarket authorities went into effect in March 2008. The FDAAA also expanded the clinical trial registry so that sponsors of all clinical trials, except for Phase 1 trials, are required to submit certain clinical trial information for inclusion in the clinical trial registry data bank. We cannot predict the likelihood, nature or extent of adverse governmental regulation, which might arise from future legislative or administrative action, either in the U.S. or abroad.

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process. If a product that has orphan drug designation subsequently receives FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication, except in very limited circumstances, for seven years. Orphan drug exclusivity, however, also could block the approval of our product for seven years if a competitor obtains approval of the same drug as defined by the FDA or if our product is determined to be contained within the competitor's product for the same indication or disease. We intend to file for orphan drug designation for those diseases or conditions that meet the criteria for orphan designation, including for PRX-08066 for the treatment of pulmonary hypertension. There is no guarantee that we will be awarded orphan designation or exclusivity for PRX-08066 or for any other products or indications. In addition, obtaining orphan drug exclusivity may not provide us with a material commercial advantage.

The FDA Modernization Act of 1997 included a pediatric exclusivity provision that was extended by the Best Pharmaceuticals for Children Act of 2002 and further extended by the FDAAA. Pediatric exclusivity is designed to provide an incentive to manufacturers for conducting research that would provide meaningful information about the safety and use of their products in children. Pediatric exclusivity, if granted, provides an additional six months of market exclusivity in the U.S. for new or currently marketed drugs. Under Section 505A of the Federal Food, Drug and Cosmetic Act, six months of market exclusivity may be granted in exchange for the voluntary completion of pediatric studies in accordance with an FDA-issued Written Request. The FDA may issue a Written Request for studies on unapproved or approved indications, where it determines that information relating to the use of a drug in a pediatric population, or part of the pediatric population, may produce health benefits in that population. We have not requested or received a Written Request for such pediatric studies, although we may ask the FDA to issue a Written Request for such studies in the future. To receive the six-month pediatric market exclusivity, we would have to receive a Written Request from the FDA, conduct the requested studies and submit reports of the studies in accordance with a written agreement with the FDA or, if there is no written agreement, in accordance with commonly accepted scientific principles, and obtain FDA acceptance of the reports of the studies. There is no guarantee that the FDA will issue a Written Request for such studies or accept the reports of the studies.

In addition to regulations in the United States, we are subject to a variety of foreign regulations governing clinical trials and the marketing of drug products. Whether or not we obtain FDA approval for a drug product, we must obtain

the necessary approvals by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The requirements governing the conduct of clinical trials and the approval processes vary from country to country and the time may be longer or shorter than that required for FDA approval.

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### **REIMBURSEMENT**

Sales of our product candidates depend in significant part on the availability of third-party reimbursement. Although we anticipate third-party payors, such as government health administrative authorities, managed care providers, private health insurers and other organizations, will provide reimbursement for our therapeutic products, significant uncertainty often exists as to the reimbursement status of newly approved health care products. Further, these third-party payors are increasingly challenging the price and examining the cost-effectiveness of medical products and services. Our product candidates may not be considered cost-effective. It is time consuming and expensive for us to seek reimbursement from third-party payors. Reimbursement may not be available or sufficient to allow us to sell our products on a competitive and profitable basis.

The passage of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, imposes new requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries, which may affect the marketing of our products. The MMA also introduced a new reimbursement methodology, part of which went into effect in 2004, and expanded the prescription drug benefit under a new Medicare Part D, which went into effect in 2006. It is not clear what effect the MMA has on the prices paid for currently approved drugs and the pricing options for new drugs. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

In addition, in some foreign countries, the proposed pricing for a product candidate must be approved before it may be lawfully marketed. The requirements governing pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market.

Several proposals to implement governmental pricing controls or reform the system of health care delivery in the United States have been considered and are currently being considered by the federal and state governments, and we expect that there will continue to be a number of such proposals at the federal and state levels. While we cannot predict whether such legislative or regulatory proposals will be adopted, the adoption of such proposals could have a material adverse effect on our business, financial condition and profitability. For example, proposals to place caps on drug prices could limit the profitability of our drug development programs, and proposals for government-funded universal health care could subject expenditures for health care to governmental budget constraints and limits on spending.

### **EMPLOYEES**

We believe that our success will depend greatly on our ability to identify, attract and retain capable employees. As of December 31, 2008, we had 91 full-time employees, 72 of which were primarily engaged in research and development activities, and 19 of which were primarily engaged in general and administrative activities. On March 12, 2009, we implemented a cost reduction initiative by reducing our workforce by approximately 44 full-time equivalent positions, affecting both research and development and general and administrative employees. Following this workforce reduction, we have 33 full-time and 4 part-time employees primarily engaged in research and development activities and 8 full-time and 4 part-time employees primarily engaged in general and administrative activities. Our employees are not represented by any collective bargaining unit.

### **RESEARCH AND DEVELOPMENT**

During the years ended December 31, 2008, 2007, and 2006 we incurred research and development expenses of \$46.2 million, \$57.5 million and \$149.8 million, respectively. Included in our 2006 research and development expense is a nonrecurring charge of \$123.5 million for the acquisition of in-process research and development in connection with our acquisition of Predix Pharmaceuticals Holdings, Inc. The in-process

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research and development charge represents the fair value of purchased in-process technology of Predix for research projects that, as of the closing date of the merger, had not reached technological feasibility and have no alternative future use.

**AVAILABLE INFORMATION**

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

**ITEM 1A. 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 will need to raise additional capital in the next five months to continue our current operations beyond the end of August 2009.*

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. As we do not have adequate funding to fund our operations beyond August 2009, we will 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.

Moreover, if our common stock is delisted from the NASDAQ Stock Market, the holders of our \$100 million aggregate principal amount of 3% Convertible Senior Notes could redeem their notes at face



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value, plus accrued and unpaid interest. We currently do not have sufficient funds to repurchase more than a nominal amount of the notes if tendered by the holders. We will need to raise significant additional capital if we become required to redeem the notes.

If we are unable to obtain significant additional capital prior to the end of August 2009, we will not be able to sustain our operations and would be required to cease our operations and/or seek bankruptcy protection. 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. Moreover, we may not have sufficient authorized shares of common stock under our certificate of incorporation to raise the significant funds necessary to continue our operations or redeem the 3% Convertible Senior Notes, if tendered. 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. Given the difficult current economic environment, we believe that it will be difficult to raise additional funds and there can be no assurance as to the availability of additional financing or the terms upon which additional financing may be available. The stock market in general, and the NASDAQ Global Market and the market for life sciences companies in particular, have recently experienced extreme price and volume fluctuations that may have been unrelated or disproportionate to the operating performance of the listed companies. There have been dramatic fluctuations in the market prices of securities of biopharmaceutical companies such as EPIX. Broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance, and may adversely impact our ability to raise additional funds. If adequate funds are not available prior to the end of August 2009, we will be unable to redeem any of our \$100 million aggregate principal amount of 3% Convertible Senior Notes, if tendered, and we would be required to cease our operations and/or seek bankruptcy protection.

***If we are not able to maintain continued listing of our common stock on the NASDAQ stock market, noteholders may require us to repurchase the \$100 million aggregate principal amount of our 3% Convertible Senior Notes.***

On November 11, 2008, we received a notice from the Listing Qualifications Staff of The NASDAQ Stock Market LLC, or the Staff, stating that we did not regain compliance with NASDAQ Marketplace Rule 4450(b)(1)(A), or the Rule, within the 30 calendar day cure period. The Rule requires a listed company to maintain stockholders' equity of at least \$10 million or a minimum market value of listed securities of \$50 million for continued listing on The NASDAQ Global Market. Pursuant to NASDAQ procedures, we requested a hearing before a NASDAQ Listing Qualifications Panel, or the Panel, which was held in December 2008. On February 4, 2009, we received notice from the Panel indicating that the Panel has determined to grant our request for continued listing on The NASDAQ Global Market, subject to the condition that on or before May 11, 2009, we file a Current Report on Form 8-K with the Securities and Exchange Commission, evidencing our compliance with the Rule. As of March 10, 2009, we were not in compliance with the Rule and there can be no assurance that we will be able to regain compliance on or prior to May 11, 2009. The Panel has the right to reconsider the terms of our continued listing based on any event, condition, or circumstance that exists or develops that would, in the opinion of the Panel, make continued listing of our securities on the NASDAQ Stock Market inadvisable or unwarranted. A delisting of our common stock from the NASDAQ Stock Market would enable the holders of our \$100 million aggregate principal amount of 3% Convertible Senior Notes to redeem their notes at face value, plus accrued and unpaid interest. We currently do not have sufficient funds to repurchase more than a nominal amount of the notes if tendered by the holders. We will need to raise significant additional capital if we become required to redeem the notes. If we are unable to acquire such additional capital, we will be unable to repurchase notes tendered for redemption, which would constitute an event of default under the indenture.

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***Our independent auditors have expressed substantial doubt about our ability to continue as a going concern, and we may be unable to raise additional capital on acceptable terms in the future.***

We have experienced significant losses since we commenced operations in 1992. Our accumulated net losses as of December 31, 2008 were approximately \$444.8 million. We have received a report from Ernst & Young LLP, our independent registered public accounting firm, regarding our consolidated financial statements as of December 31, 2008 and for the fiscal year then ended, which included an explanatory paragraph stating that the financial statements were prepared assuming we will continue as a going concern. The report also stated that our recurring operating losses and need for additional financing have raised substantial doubt about our ability to continue as a going concern. As we do not have adequate funding to fund our operations beyond August 2009, we will need to raise substantial additional funds for research, development and other expenses through equity or debt financings, strategic alliances or otherwise. Given the difficult current economic environment, we believe that it will be difficult to raise additional funds and there can be no assurance as to the availability of additional financing or the terms upon which additional financing may be available. In addition, the going concern explanatory paragraph included in our auditor's report on our consolidated financial statements could inhibit our ability to enter into strategic alliances or other collaborations or our ability to raise additional financing. If we are unable to obtain such additional capital, we will not be able to sustain our operations and would be required to cease our operations and/or seek bankruptcy protection. Additionally, even if we do raise sufficient capital and generate revenues to support our operating expenses beyond August 2009, there can be no assurances that the revenue will be sufficient to enable us to develop our business to a level where it will generate profits and cash flows from operations. In addition, 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 obtain additional debt financing, a substantial portion of our operating cash flow may be dedicated to the payment of principal and interest on such indebtedness, and the terms of the debt securities issued could impose significant restrictions on our operations.

***We may not be able to monetize our commercial rights to Vasovist, which would have a material adverse effect on our business.***

Our blood-pool magnetic resonance angiography imaging agent, Vasovist, was approved for marketing in the United States in December 2008 and has been approved for marketing in over 30 countries outside of the United States. In September 2008, Bayer Schering terminated its strategic collaboration agreement with us effective March 1, 2009. Accordingly, the worldwide commercial rights for Vasovist were transferred back to us on such date. Our current intention is to monetize the commercial rights to Vasovist to help fund our operations. As a result of Bayer Schering's termination of the collaboration agreement, we cannot assure you that we would be able to find another collaborator to commercialize Vasovist. Our ability to successfully monetize our commercial rights to Vasovist will be partially dependent on historical sales of Vasovist by Bayer Schering outside the United States. 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 commercial rights, and our failure to do so could materially and adversely affect our ability to generate revenues. Moreover, upon entering into a collaboration agreement for the commercialization of Vasovist, we would be obligated under our prior collaboration agreement to pay Bayer Schering for a portion of their development costs. The reimbursement will be based on pre-defined percentages of the development costs, allocated to each territory for which the commercial rights are sold, with full worldwide rights amounting to a \$33 million reimbursement to Bayer Schering. We cannot assure you that we would be able to monetize the commercial rights for an amount that is greater than the amount that would be due to Bayer Schering. Disagreements with Bayer Schering regarding intellectual property rights or the transfer of information regarding Vasovist could also delay or terminate our efforts to successfully monetize our commercial rights to Vasovist. In addition, Covidien is currently the only manufacturer approved by the FDA to produce Vasovist. Covidien's agreement may be required for us to monetize Vasovist, and we cannot assure you that Covidien would be willing to manufacture Vasovist on terms acceptable to us

or any potential third-party acquirer of the commercial rights to Vasovist. Our failure to successfully monetize Vasovist on or prior to the end of August

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2009 would materially harm our ability to sustain our operations, and we could be forced to seek bankruptcy protection.

***We significantly increased our leverage as a result of the issuance of 3% Convertible Senior Notes due 2024, and may be unable to repay, repurchase or redeem these notes if, and when, required.***

In connection with the issuance of 3% 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. 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 or termination of trading of our common stock on the NASDAQ Stock Market.

In February 2009, a NASDAQ Listing Qualifications Panel, or the Panel, determined to grant our request for continued listing on The NASDAQ Global Market, subject to the condition that on or before May 11, 2009, we file a Current Report on Form 8-K with the Securities and Exchange Commission, evidencing our compliance with NASDAQ Marketplace Rule 4450(b)(1)(A). NASDAQ Marketplace Rule 4450(b)(1)(A) requires the company to maintain a stockholders' equity of at least \$10 million or a minimum market value of listed securities of \$50 million. As of March 10, 2009, we were not in compliance with the Rule and there can be no assurance that we will be able to regain compliance on or prior to May 11, 2009. The Panel has the right to reconsider the terms of our continued listing based on any event, condition, or circumstance that exists or develops that would, in the opinion of the Panel, make continued listing of our securities on the NASDAQ Stock Market inadvisable or unwarranted. A delisting of our common stock from the NASDAQ Stock Market would enable the holders of our \$100 million aggregate principal amount of 3% Convertible Senior Notes to redeem their notes at face value, plus accrued and unpaid interest. We currently do not have sufficient funds to repurchase more than a nominal amount of the notes if tendered by the holders. We will need to raise significant additional capital if we become required to redeem the notes. If we are unable to acquire such additional capital, we will be unable to repurchase notes tendered for redemption, which would constitute an event of default under the indenture.

Even if we are able to maintain our listing on the NASDAQ Stock Market, 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.

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

Our future financial results are uncertain. We have experienced significant losses since we commenced operations in 1992. Our accumulated net losses as of December 31, 2008 were approximately \$444.8 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.

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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.

***A substantial portion of our future revenues will be dependent upon our agreements with GlaxoSmithKline, CFFT and Amgen Inc.***

We expect that a substantial portion of our future revenues will be dependent upon our collaboration agreements with GlaxoSmithKline, CFFT and Amgen Inc. The agreement with GlaxoSmithKline encompasses the development and commercialization of compounds targeting four G-protein coupled receptors, or GPCRs, for the treatment of a variety of diseases, including an option to license our 5-HT<sub>4</sub> partial agonist, PRX-03140, and other compounds arising from the four research programs. The agreement with CFFT encompasses the development and commercialization of at least one compound to correct a malfunction of the cystic fibrosis transmembrane conductance regulator protein. 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. 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, CFFT and Amgen 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 GlaxoSmithKline and Amgen 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. In addition, 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. If any of our agreements with GlaxoSmithKline, CFFT or Amgen 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. For instance, effective March 1, 2009, Bayer Schering terminated its strategic collaboration agreement with us with respect to Vasovist. 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, or to otherwise monetize Vasovist, and our failure to do so could materially and adversely affect our ability to generate revenues.

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

We have never had a therapeutic product candidate 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 March 2008, results from our Phase 2b clinical trial of our PRX-00023 product candidate for major depressive disorder demonstrated that PRX-00023 did not achieve a statistically significant improvement over placebo for the primary endpoint with respect to major depressive disorder. Prior to obtaining results from this trial, PRX-00023 was our most advanced therapeutic drug candidate. Based on these trial results, however, we discontinued our development efforts with respect to PRX-00023.

In addition, each of our current clinical-stage therapeutic drug candidates in the United States requires additional clinical studies: PRX-03140 for the treatment of Alzheimer's disease, PRX-08066 for the treatment

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

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

To date, we have received revenues from payments made under licensing, royalty arrangements and product development and marketing agreements with strategic collaborators. In particular, our revenue for the twelve months ended December 31, 2008 was \$28.6 million and consisted of \$26.2 million of product development revenue from GlaxoSmithKline, CFFT and Bayer Schering, \$0.6 million of royalty revenue related to the Bayer Schering agreement, and \$1.8 million of license fee revenue related to the GlaxoSmithKline, CFFT, Bayer Schering 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. Although we are eligible for additional payments under our agreements with GlaxoSmithKline, Amgen and CFFT, we do not expect any such payments will extend our available cash beyond the end of August 2009. 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

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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, effective March 1, 2009, Bayer Schering terminated its strategic collaboration agreement with us with respect to Vasovist. Accordingly, the worldwide commercial rights for Vasovist were transferred back to us on such date. It is our intention to sell the commercial rights to Vasovist. However, there is no guarantee that we will be able to do so. 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

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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;

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.

***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

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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 efficacy of the product candidate. If approval of an application to market product candidates is not granted on a timely basis or at all, or if we are unable to maintain our approval, our business may be materially harmed. It is possible that none of our product candidates or any other product candidates we may seek to develop in the future will ever obtain the appropriate regulatory approvals necessary for us to begin selling them, which would materially harm our business.

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

We will only receive regulatory approval to commercialize a product candidate if we can demonstrate to the satisfaction of the FDA or the applicable foreign regulatory agency, in well-designed and conducted clinical trials, that the product candidate is safe and effective and otherwise meets the appropriate standards required for approval for a particular indication. Clinical trials are lengthy, complex and extremely expensive processes with uncertain results. For example, results from our completed Phase 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. 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;

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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.

***Gadolinium-based imaging agents, such as Vasovist, may cause adverse side effects which could limit our ability to sell our commercial rights to Vasovist.***

Vasovist is a contrast agent 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 sell the commercial rights to 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 is safe and effective. We may not be able to enroll a sufficient number of qualified patients in a timely or cost-effective manner. For

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example, we are experiencing difficulty in enrolling subjects in our current Phase 2b clinical trial for PRX-08066. 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 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);

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

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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. For instance, the Securities and Exchange Commission commenced an informal investigation regarding our stock option grants. 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 therapeutic product candidates outside the United States vary greatly from country to country and may require additional testing. Although we obtained regulatory approval of Vasovist in the United States, we have no experience in obtaining regulatory approvals for any of our product candidates outside of the United States. 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.

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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 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;

finest;

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

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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.

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 Medivation, 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 more than 100 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 hypertension in association with chronic obstructive pulmonary disease, 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 Bayer Schering Pharma AG, Germany. We believe that there are more than 15 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), 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 more than 60 therapeutic product candidates in clinical trials for the treatment of cognitive impairment in association with schizophrenia.

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

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compete with Vasovist. Such products include Magnevist and Gadovist by Bayer Schering Pharma AG, Germany, Dotarem by Guerbet, S.A., Omniscan by GE Healthcare, ProHance and MultiHance by Bracco and OptiMARK by Covidien Ltd. We are aware of six agents under clinical development that have been or are being evaluated for use in magnetic resonance angiography: Bayer Schering'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 Ferumoxylol. 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.

***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.

***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. Covidien is

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currently the only manufacturer approved by the FDA to produce Vasovist. Covidien's agreement may be required for us to monetize Vasovist, and we cannot assure you that Covidien would be willing to manufacture Vasovist on terms acceptable to us or any potential third-party acquirer of the commercial rights to 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.

***If we are unable to attract and retain key management and other personnel, it would hurt our ability to operate effectively and execute our business strategy.***

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, in July 2008, Michael G. Kauffman, M.D., Ph.D. resigned his position as our Chief Executive Officer, and in February 2009, Chen Schor announced his resignation as our Chief Business Officer, effective March 23, 2009. Drs. Uprichard and Kauffman and Mr. Schor have been critical to the pursuit of our business goals and we may experience difficulties implementing our business strategy following their respective departures. In addition, on March 12, 2009 we implemented a cost reduction initiative that eliminated approximately 44 full-time equivalent positions, including the termination of 2 members of our senior management team and the reduction to part-time status of 2 other members of our senior management team. The loss of these and any of our other key personnel, or the failure of our remaining key personnel 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

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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, the requirements of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 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.

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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 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 (wholly or jointly) or license patents and patent applications on aspects of our core technology as well as many



specific applications of this technology. As of February 2009, our patent portfolio included a total of 18 issued U.S. patents, 129 issued foreign patents, and 275 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 and Vasovist. We also exclusively license technology embodied in patent applications from Ramot at Tel Aviv University Ltd., the technology transfer

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company of Tel Aviv University. 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, if we lose this license, 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 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. If we fail to comply with our obligations under this license agreement, the license could convert from exclusive to nonexclusive, or terminate entirely. It is unlikely that we would be able to obtain the technology licensed under this agreement elsewhere, 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 the 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



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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 product candidates. 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.

**RISKS RELATED TO OUR SECURITIES**

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

The stock market in general, and the NASDAQ Global Market and the market for life sciences companies in particular, have recently experienced extreme price and volume fluctuations that may have been unrelated or disproportionate to the operating performance of the listed companies. The market price of our common stock is affected by these general market conditions as well as numerous other 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;

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the timing of our achievement of regulatory milestones;

conditions and trends in the pharmaceutical and other technology industries;

adoption of new accounting standards affecting such industries;

changes in financial estimates by securities analysts;

perceptions of the value of corporate transactions; and

degree of trading liquidity in our common stock and general market conditions.

From the closing of our merger with Predix and our 1 for 1.5 share reverse stock split on August 16, 2006 to March 10, 2009, the closing price of our common stock ranged from \$0.22 to \$7.58 per share. The last reported closing price for our common stock on March 10, 2009 was \$0.48. The significant decline 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.

The stock market in general, and the NASDAQ Global Market and the market for life sciences companies in particular, have recently experienced extreme price and volume fluctuations that may have been unrelated or disproportionate to the operating performance of the listed companies. There have been dramatic fluctuations in the market prices of securities of biopharmaceutical companies such as EPIX. 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 lawsuit 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.

***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.

**ITEM 1B. *UNRESOLVED STAFF COMMENTS***

None.

**Table of Contents****ITEM 2. PROPERTIES**

We lease a total of 57,300 square feet of space at our 4 Maguire Road, Lexington, Massachusetts location and 9,200 square feet of space at our 3 Hayetzira Street, Ramat Gan, Israel location. The lease at 4 Maguire Road expires October 2013 and the lease at 3 Hayetzira Street, Israel expires January 31, 2010. We believe that our current facilities are adequate to meet our needs until the expiration of the leases.

**ITEM 3. LEGAL PROCEEDINGS**

From time to time we are a party to various legal proceedings arising in the ordinary course of our business. In addition, we have in the past been, and may in the future be, subject to investigations by regulatory authorities which expose us to greater risks associated with litigation, regulatory, or other proceedings, as a result of which we could be required to pay significant fines or penalties. The outcome of litigation, regulatory or other proceedings cannot be predicted with certainty and some lawsuits, claims, actions or proceedings may be disposed of unfavorably to us. In addition, intellectual property disputes often have a risk of injunctive relief which, if imposed against us, could materially and adversely affect our financial condition, or results of operations. From time to time, third-parties have asserted and may in the future assert intellectual property rights to technologies that are important to our business and have demanded and may in the future demand that we license their technology.

**ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS**

No matters were submitted to a vote of our security holders, whether through the solicitation of proxies or otherwise, during our 2008 fourth fiscal quarter.

**PART II****ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES**

Our Common Stock is listed on The NASDAQ Global Market under the symbol EPIX.

The following table sets forth, for the periods indicated, the range of the high and low sales prices for our Common Stock as reported on The NASDAQ Global Market:

	<b>High</b>	<b>Low</b>
<b>2007</b>		
First Quarter	\$ 7.20	\$ 6.08
Second Quarter	7.28	5.08
Third Quarter	5.90	3.67
Fourth Quarter	5.40	2.89
<b>2008</b>		
First Quarter	4.41	1.33
Second Quarter	2.50	1.28
Third Quarter	2.16	0.84
Fourth Quarter	1.87	0.21



The above quotations reflect inter-dealer prices without retail mark-up, markdown or commission and may not necessarily represent actual transactions.

On March 10, 2009, the last reported price for the common stock was \$0.48 per share. As of March 10, 2009, there were 168 holders of record of the 41,947,441 outstanding shares of Common Stock. To date, we have neither declared nor paid any cash dividends on shares of our Common Stock and do not anticipate doing so for the foreseeable future.

**Table of Contents****ISSUER PURCHASES OF EQUITY SECURITIES**

The following table sets forth the repurchases of our equity securities during the three months ended December 31, 2008 by or on behalf of us or any affiliated purchaser:

<b>Period(1)</b>	<b>(a) Total number of Shares (or Units) Purchased</b>	<b>(b) Average Price Paid per Share (or Unit)</b>
Fiscal month beginning December 1, 2008 and ended December 31, 2008	165,344(2)	\$ 1.03(3)
Total	165,344(2)	\$ 1.03(3)

- (1) There were no other repurchases of our equity securities by or on behalf of us or any affiliated purchaser during the three months ended December 31, 2008.
- (2) With respect to grants of stock in December 2008 to certain employees, we repurchased from the employees a number of shares of stock with a value, based on the fair market value on the date of grant, equal to our required minimum income tax withholding obligation for the shares. Shares repurchased under this arrangement are not available for future awards under our 2008 Stock Option and Incentive Plan.
- (3) The amount represents the last reported sale price of our common stock on The NASDAQ Global Market on December 31, 2008.

**ITEM 6. SELECTED FINANCIAL DATA**

The following table sets forth consolidated financial data for each of the five years in the period ending December 31, 2008. In thousands, except per share data.

The information below should be read in conjunction with the consolidated financial statements (and notes thereon) and Management's Discussion and Analysis of Financial Condition and Results of Operations, included in Item 7.

	<b>Year Ended December 31,</b>				
	<b>2008</b>	<b>2007</b>	<b>2006(1)</b>	<b>2005</b>	<b>2004</b>
<b>Statement of Operations Data:</b>					
Revenues	\$ 28,628	\$ 14,960	\$ 6,041	\$ 7,190	\$ 12,259
Operating loss	(34,241)	(63,564)	(157,668)	(21,760)	(22,351)
Net loss	(36,671)	(62,789)	(157,393)	(21,269)	(22,621)
Weighted average common shares outstanding:					
Basic and diluted	41,466	33,936	20,789	15,505	15,259
Net loss per share, basic and diluted	\$ (0.88)	\$ (1.85)	\$ (7.57)	\$ (1.37)	\$ (1.48)

	2008	2007	December 31, 2006	2005	2004
<b>Balance Sheet Data:</b>					
Cash, cash equivalents and marketable securities	\$ 24,597	\$ 61,077	\$ 109,543	\$ 124,728	\$ 164,440
Total assets	41,069	78,075	125,027	130,716	171,287
Convertible debt(2)	100,000	100,000	100,000	100,000	100,000
Long-term liabilities	118,276	120,846	120,066	100,756	101,210

(1) We merged with Predix on August 16, 2006. 2006 includes a charge of \$123.5 million for acquired in-process research and development related to the merger.

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- (2) Noteholders may require us to repurchase the notes at par, plus accrued and unpaid interest, on June 15, 2011, 2014 and 2019 and upon certain other events, including a change of control and termination of trading of our common stock on the NASDAQ Stock Market.

**ITEM 7. *MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS***

The information contained in this section has been derived from our consolidated financial statements and should be read together with our consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K.

**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. We also have collaborations with SmithKline Beecham Corporation (GlaxoSmithKline), Amgen Inc., and Cystic Fibrosis Foundation Therapeutics, Incorporated, or CFFT.

Since our acquisition of Predix Pharmaceuticals Holdings, Inc., or Predix, in August 2006, our focus has been on the development of therapeutic drug products. 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 typically 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 blood-pool magnetic resonance angiography imaging agent, Vasovist, was approved by the U.S. Food and Drug Administration, or FDA, for marketing in the United States in December 2008, and has been approved for marketing in over 30 countries outside of the United States. In September 2008, Bayer Schering Pharma AG, Germany, or Bayer Schering, terminated the strategic collaboration agreement between us and Bayer Schering relating to Vasovist, effective March 1, 2009. Accordingly, the worldwide commercial rights for Vasovist were transferred back to us on such date. It is our intention to sell the commercial rights to Vasovist. However, there is no guarantee that we will be able to do so. Upon a sale of the commercial rights to Vasovist, we will be required to reimburse Bayer Schering for a portion of their development costs. The reimbursement will be based on pre-defined percentages of the development costs, allocated to each territory for which the commercial rights are sold, with full worldwide rights amounting to a \$33 million reimbursement to Bayer Schering.

We have experienced and continue to experience negative cash flows from operations and we expect to continue to incur net losses in the foreseeable future. Accordingly, in March 2009 and October 2008, we implemented workforce reductions that eliminated approximately 62% of our workforce in connection with our efforts to reduce our cost

structure. These workforce reductions are expected to reduce our annual salary and benefit costs by approximately \$7.4 million. We also narrowed the focus of our research and development efforts to our lead clinical programs, PRX-03140 being developed for the treatment of Alzheimer's disease and PRX-08066 being developed for the treatment of pulmonary hypertension associated with chronic obstructive pulmonary disease (COPD), as well as our partnered preclinical programs with GlaxoSmithKline and CFFT. In

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connection with the March 2009 workforce reduction, we entered into a letter agreement with GlaxoSmithKline allowing us to reduce our research and development obligations under our collaboration agreement, during the period from March 13, 2009 to September 13, 2009, for programs other than the PRX-03140 program.

As of December 31, 2008, we had \$24.6 million of cash and cash equivalents to fund our future operations. We believe that our cash and cash equivalents, along with anticipated revenue that we expect to earn during the first half of 2009, will fund our operations only through the end of August 2009. In addition, on February 4, 2009, we received notice from the Listing Qualifications Panel of the NASDAQ Stock Market LLC, or NASDAQ, that it has determined to continue the listing of our common stock on the NASDAQ Global Market subject to our compliance with Marketplace Rule 4450(b)(1)(A), which requires us to maintain a market value of our common stock of at least \$50,000,000 for at least 10 consecutive days on or prior to May 11, 2009. As of March 10, 2009, we were not in compliance with the requirement for continued inclusion on NASDAQ. If we do not regain compliance with the rules for continued listing on NASDAQ, our common stock will be delisted from NASDAQ. If our common stock is delisted from NASDAQ, the holders of our \$100 million aggregate principal amount of 3% Convertible Senior Notes could redeem their notes at face value, plus accrued and unpaid interest. We currently do not have sufficient funds to repurchase more than a nominal amount of the notes if tendered by the holders. Accordingly, we will need to raise significant additional capital to fund our operations beyond August 2009 or if we are required to redeem the notes. If we are unable to obtain such additional capital, we will not be able to sustain our operations and would be required to cease our operations and/or seek bankruptcy protection. Given the difficult current economic environment, we believe that it will be difficult for companies such as ours to raise additional funds and there can be no assurance as to the availability of additional financing or the terms upon which additional financing may be available. As a result of our recurring operating losses and need for additional financing, the audit report relating to our consolidated financial statements as of and for the year ended December 31, 2008 contains an explanatory paragraph regarding substantial doubt about our ability to continue as a going concern.

## **Critical Accounting Policies And Estimates**

The discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect our reported assets and liabilities, revenues and expenses, and other financial information. These items are monitored and analyzed by management for changes in facts and circumstances, and material changes in these estimates could occur in the future. Changes in estimates are reflected in reported results for the period in which they become known. We base our estimates on historical experience and various other assumptions that we believe to be reasonable under the circumstances. Actual results may differ significantly from the estimates under different assumptions and conditions.

We believe that our accounting policies related to revenue recognition, research and development and employee stock compensation, as described below, require significant estimates and judgments on the part of management. Our significant accounting policies, including the ones described below, are more fully described in Note 2 of our Consolidated Financial Statements for the year ended December 31, 2008.

### ***Revenue Recognition***

We recognize revenue relating to collaborations in accordance with the Securities and Exchange Commission's, or SEC's, Staff Accounting Bulletin (SAB) No. 104, *Revenue Recognition*, or SAB 104. Revenue under collaborations may include the receipt of non-refundable license fees, milestone payments, reimbursement of research and development costs and royalties.

We recognize nonrefundable upfront license fees and guaranteed, time-based payments that require continuing involvement in the form of research and development as license fee revenue ratably over the development period. When the period of deferral cannot be specifically identified from the contract, we estimate the period based upon other critical factors contained within the contract. We continually review such

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estimates which could result in a change in the deferral period and might impact the timing and amount of revenue recognized.

Milestone payments which represent a significant performance risk are recognized as product development revenue when the performance obligations, as defined in the contract, are achieved. Performance obligations typically consist of significant milestones in the development life cycle of the product candidate, such as the filing of investigational new drug applications, initiation of clinical trials, filing for approval with regulatory agencies and approvals by regulatory agencies. Milestone payments that do not represent a significant performance risk are recognized ratably over the development period.

Reimbursements of research and development costs are recognized as product development revenue as the related costs are incurred.

Royalties are recognized as revenue when earned, reasonably estimable and collection is probable, which is typically upon receipt of royalty reports from the licensee or cash.

### ***Product development revenue***

We recognize as revenue from GlaxoSmithKline and CFFT certain third-party costs incurred by us and internal development efforts in the performance of research activities under the related contracts. Internal development efforts are billed at standard rates under the contracts. This revenue is recognized in the same period in which the costs are incurred.

We recognize as revenue from Bayer Schering costs incurred by us in excess of our obligation under the agreement to expend 50% of the costs to develop Vasovist. This revenue is recognized in the same period in which the costs are incurred. With respect to payments due to Bayer Schering, if any, in connection with the Vasovist development program, we recognize such amounts as a reduction in revenue at the time Bayer Schering performs the research and development activities for which we are obligated to pay Bayer Schering. Costs to develop Vasovist were essentially completed in December 2008 upon the approval of Vasovist by the Food and Drug Administration, or FDA, for marketing in the United States.

### ***Royalty revenue***

We are entitled to receive a royalty on worldwide sales of Primovist and on sales of Vasovist outside of the United States (through March 1, 2009) by Bayer Schering. Royalty revenue is recognized in the period in which royalty reports are received and are based on actual revenues or gross profits as reported to us by Bayer Schering.

### ***License fee revenue***

We recognize revenue from non-refundable license fees and milestone payments, not specifically tied to a separate earnings process, ratably over the period during which we have a substantial continuing obligation to perform services under the contract. Certain contracts require judgment to determine the period of continuing involvement by us and these estimates are subject to change based upon changes in facts and circumstances. When milestone payments are specifically tied to a separate earnings process, revenue is recognized when the specific performance obligations associated with the payment are completed.

### ***Research and Development***



We account for research and development costs in accordance with Statement of Financial Accounting Standards (SFAS) No. 2, *Accounting for Research and Development Cost*, which requires that expenditures be expensed to operations as incurred.

Research and development expenses primarily include employee salaries and related costs, third-party service costs, the cost of preclinical and clinical trials, supplies, consulting expenses, facility costs and certain overhead costs.

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In order to conduct research and development activities and compile regulatory submissions, we enter into contracts with vendors who render services over extended periods of time. Typically, we enter into three types of vendor contracts: time-based, patient-based or a combination thereof. Under a time-based contract, using critical factors contained within the contract, usually the stated duration of the contract and the timing of services provided, we record the contractual expense for each service provided under the contract ratably over the period during which we estimate the service will be performed. Under a patient-based contract, we first determine an appropriate per patient cost using critical factors contained within the contract, which include the estimated number of patients and the total dollar value of the contract. We then record expense based upon the total number of patients enrolled in the clinical study ratably during the treatment period. On a quarterly basis, we review the assumptions for each contract in order to reflect our most current estimate of the costs incurred under each contract. Adjustments are recorded in the period in which the revisions are estimable. These adjustments could have a material effect on our results of operations.

### ***Employee Stock Compensation***

We apply the provisions of SFAS No. 123(R), *Share-Based Payment – An Amendment of FASB Statements No. 123 and 95*, or SFAS 123(R), to our share-based payments.

Determining the appropriate fair value model and calculating the fair value of share-based awards requires us to make various judgments, including estimating the expected life of the share-based award, the expected stock price volatility over the expected life of the share-based award and forfeiture rates. In order to determine the fair value of share-based awards on the date of grant, we use the Black-Scholes option-pricing model. Inherent in this model are assumptions related to stock price volatility, option life, risk-free interest rate and dividend yield. The risk-free interest rate is a less subjective assumption as it is based on treasury instruments whose term is consistent with the expected life of options. We use a dividend yield of zero as we have never paid cash dividends and have no intention to pay cash dividends in the foreseeable future. The stock price volatility and option life assumptions require a greater level of judgment. Estimating forfeitures also requires significant judgment. Our stock-price volatility assumption is based on trends in both our current and historical volatilities of our stock. We estimate the expected term of options primarily based upon our historical experience of the holding period prior to the exercise or expiration of a vested option. We estimate forfeitures based on our historical experience of cancellations of share-based compensation prior to vesting. We believe that our estimates are based on outcomes that are reasonably likely to occur. To the extent actual forfeitures differ from our estimates, we will record an adjustment in the period the estimates are revised.

## **Results of Operations**

### ***Research and Development Overview***

We have experienced and continue to experience negative cash flows from operations and we expect to continue to incur net losses in the foreseeable future. Accordingly, in March 2009 and October 2008, we implemented workforce reductions that eliminated approximately 62% of our workforce in connection with our efforts to reduce our cost structure. We also narrowed the focus of our research and development efforts to our lead clinical programs, PRX-03140 being developed for the treatment of Alzheimer's disease and PRX-08066 being developed for the treatment of pulmonary hypertension associated with COPD, as well as our partnered preclinical programs with GlaxoSmithKline and CFFT.

Research and development expense consists primarily of:

salaries, benefits and related expenses for personnel engaged in research and development activities;

fees paid to contract research organizations to manage and monitor clinical trials;

fees paid to the investigator sites who participate in clinical trials;

fees paid to research organizations in conjunction with preclinical studies;

costs of materials used in research and development and clinical studies;

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fees paid to access chemical and intellectual property databases;

academic testing and consulting, license and sponsored research fees paid to third parties; and

costs of facilities and equipment, including depreciation, used in research and development activities.

We expense both internal and external research and development costs as incurred. These expenditures are subject to numerous uncertainties in timing and cost to completion. We test drug candidates in preclinical studies for safety, toxicology and efficacy. We then conduct early-stage clinical trials for each drug candidate. As we obtain results from trials, we may elect to discontinue or delay clinical trials for certain drug candidates in order to focus our resources on more promising drug candidates.

In connection with our acquisition of Predix Pharmaceuticals Holdings, Inc. in August 2006, we incurred a non-recurring charge of \$123.5 million for in-process research and development. The in-process research and development charge represents the fair value of purchased in-process technology of Predix for research projects that, as of the closing date of the merger, had not reached technological feasibility and had no alternative future use. The in-process research and development primarily represented the fair value of the following drug candidates: PRX-00023 (\$70.9 million) that, as of the date of the merger, was in Phase 3 clinical trials for the treatment of generalized anxiety disorder; PRX-03140 (\$23.5 million) that, as of the date of the merger had completed Phase 1 clinical trials for the treatment of Alzheimer's disease; PRX-08066 (\$20.2 million) that, as of the date of the merger, had entered Phase 2 clinical trials for the treatment of pulmonary hypertension in association with chronic obstructive pulmonary disease, or COPD; and PRX-07034 (\$8.9 million) that, as of the date of the merger, had entered Phase 1 clinical trials. In March 2008, we discontinued the development of PRX-00023 due to a lack of efficacy shown in a Phase 2b trial in patients with major depressive disorder.

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

<b>Drug Candidate</b>	<b>Disease Indication</b>	<b>Clinical Trial Status</b>
PRX-03140(1)	Alzheimer's disease	Phase 2b
PRX-08066(2)	Pulmonary Hypertension/COPD	Phase 2b
PRX-07034(3)	Cognitive impairment in association with schizophrenia	Phase 1b

(1) In May 2008, we initiated a Phase 2b trial in Alzheimer's disease of PRX-03140 in combination with Aricept (donepezil). 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 alone 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; 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 also includes a three-month optional extension.

- (2) In August 2008, we initiated a Phase 2b right-heart catheter study of PRX-08066 in patients with COPD and moderate-to-severe pulmonary hypertension (PH). This single-arm, open-label, Phase 2b 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

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day one of the trial followed by twice-daily dosing of 300 mg of PRX-08066 for three months. The trial is designed to enroll adult patients with COPD and moderate-to-severe PH.

- (3) PRX-07034 has completed multiple Phase 1 studies and is being developed for the treatment of cognitive impairment in association with schizophrenia. We put development of this program on hold as part of a cost reduction initiative implemented in October 2008. Future development of this program is dependent upon us raising a significant amount of capital.

Completion of clinical trials may take several years or more, but the length of time can vary substantially according to a number of factors, including the type, complexity, novelty and intended use of a drug candidate. The cost of clinical trials, and therefore the amount and timing of our capital requirements, may vary significantly over the life of a project as a result of differences arising during clinical development, including, among others:

the number of patients that participate in the trials;

the length of time required to enroll suitable patient subjects;

the number of sites included in the trials;

the duration of patient follow-up that seems appropriate in view of results; and

the efficacy and safety profile of the drug candidate.

We could incur increased clinical development costs if we experience delays in clinical trial enrollment, delays in the evaluation of clinical trial results or delays in regulatory approvals. In addition, we face significant uncertainty with respect to our ability to enter into strategic collaborations with respect to our drug candidates. As a result of these factors, it is difficult to estimate the cost and length of a clinical trial. We are unable to accurately and meaningfully estimate the cost to bring a product to market due to the variability in length of time to develop and obtain regulatory approval for a drug candidate.

We estimate that clinical trials in our areas of focus are typically completed over the following timelines, but delays can occur for many reasons including those set forth above:

<b>Clinical Phase</b>	<b>Objective</b>	<b>Estimated Completion Period</b>
Phase 1	Establish safety in healthy volunteers and occasionally in patients; study how the drug works, is metabolized and interacts with other drugs	1-2 years
Phase 2	Evaluate efficacy, optimal dosages and expanded evidence of safety	2-3 years
Phase 3	Further evaluate efficacy and safety of the drug candidate in a larger patient population	2-3 years

If we successfully complete Phase 3 clinical trials of a drug candidate, we intend to submit the results of all of the clinical trials for such drug candidate to the FDA to support regulatory approval. Even if any of our drug candidates receive regulatory approval, we may still be required to perform lengthy and costly post-marketing studies. In addition, we currently have no commercial manufacturing, marketing, sales or distribution capabilities. To commercialize any of our drug candidates we would have to develop these capabilities internally or through

collaboration with third parties.

A major risk associated with the timely completion and commercialization of our drug candidates is the ability to confirm safety and efficacy based on the data of long-term clinical trials. For instance, in March 2008, we discontinued development of PRX-00023 due to lack of efficacy shown in a Phase 2b trial in patients with major depressive disorder. We cannot be certain that any of our drug candidates will prove to be safe or effective, will receive regulatory approvals or will be successfully commercialized. In order to achieve marketing approval, the FDA or foreign regulatory agencies must conclude that our clinical data establishes the safety and efficacy of our drug candidates. If our clinical-stage drug candidates are not successfully developed, future results of operations may be adversely affected.

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We do not budget or manage our research and development costs by project on a fully allocated basis. Consequently, fully allocated research and development costs by project are not available. We use our employee and infrastructure resources across several projects and many of our costs are not attributable to an individually-named project but are directed to broadly applicable research projects. As a result, we cannot state precisely the costs incurred for each of our clinical projects on a project-by-project basis. We estimate that, from the date we acquired Predix, August 16, 2006, through December 31, 2008, total third-party costs incurred for preclinical study support, clinical supplies and clinical trials associated with our three therapeutic clinical programs are as follows:

PRX-03140	\$ 17.7 million
PRX-08066	\$ 5.5 million
PRX-07034	\$ 9.8 million

As a result of the uncertainties discussed above, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent we will receive cash inflows from the commercialization and sale of a product. For example, we have suspended further development of PRX-07034 as part of a cost reduction initiative implemented in October 2008.

**Financial Results*****Years ended December 31, 2008 and 2007****Revenue*

The following table presents revenue and revenue growth (decline) for the years ended December 31, 2008 and 2007:

	<b>Years Ended December 31,</b>		<b>2007</b>
	<b>2008</b>	<b>Increase (Decrease)</b>	
	<b>Revenue</b>		<b>Revenue</b>
Product development revenue	\$ 26,190,203	156%	\$ 10,239,120
Royalty revenue	626,228	(38)%	1,017,669
License fee revenue	1,811,924	(51)%	3,703,260
Total	\$ 28,628,355	91%	\$ 14,960,049

Our revenue to date has consisted principally of product development revenue under our collaboration agreements with GlaxoSmithKline, CFFT, and Bayer Schering (for imaging programs); from license fee revenue relating to our agreements with Amgen, GlaxoSmithKline, Bayer Schering, CFFT, Covidien and Bracco; and from royalties related to our agreements with Bracco and Bayer Schering. Royalties from Bracco concluded in the second quarter of 2007.

Product development revenue increased 156% in the year ended December 31, 2008 compared to the prior year primarily as a result of an increase of \$5.8 million in milestones achieved from our collaboration agreements with GlaxoSmithKline and CFFT, as well as increased revenue in 2008 from reimbursed research costs earned under both of these agreements. The 2008 period includes \$13.5 million of milestones earned for specific achievements in 2008 as provided for in the collaboration agreements. The 2008 period also includes approximately \$1.0 million of revenue



related to the development of Vasovist, which was essentially completed in 2008.

The decrease in royalty revenue of 38% in the year ended December 31, 2008 compared to the prior year was primarily due to a reduction in royalties on sales of MultiHance by Bracco due to the expiration of patents. The 2008 period includes approximately \$0.5 million of royalties for sales of Vasovist outside of the United States. We will stop receiving royalties on Vasovist sales effective upon the termination of our collaboration agreement with Bayer Schering on March 1, 2009.

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License fee revenue decreased 51% in the year ended December 31, 2008 compared to the prior year primarily as a result of a decrease in the recognition of deferred revenue from the Amgen collaboration agreement. The deferred revenue from our Amgen agreement was fully recognized in October 2007 when we completed our research obligation. Partially offsetting this decrease was an increase of \$0.5 million in deferred revenue recognition relating to the termination of the Bayer Schering collaboration agreement effective March 1, 2009.

### *Research and Development Expense*

Research and development expense of \$46.2 million for the year ended December 31, 2008 reflects a decrease of \$11.3 million or 20% from the prior year. The decrease in research and development expense during 2008 was primarily due to a decrease of \$17.2 million in third-party expenses associated with our clinical development programs. The decrease in our clinical program expense was largely due to the discontinuation of our PRX-00023 program in March 2008 and our decision to suspend further development of our PRX-07034 program in October 2008. These decreases were partially offset by increased costs to support our preclinical programs during the period. Clinical program costs incurred in 2008 include costs for the two ongoing Phase 2b clinical trials of PRX-03140 for Alzheimer's disease, the ongoing Phase 2b clinical trial of PRX-08066 for chronic obstructive pulmonary disease and moderate-to-severe pulmonary hypertension, the completion in the first half of 2008 of the Phase 2b clinical trial of PRX-00023 for depression and the costs related to the new drug application (NDA) resubmission for Vasovist.

### *General and Administrative Expense*

General and administrative expense of \$13.0 million for the year ended December 31, 2008 reflects a decrease of \$7.0 million or 35% from the prior year. The decrease in general and administrative expense during 2008 was primarily due to \$5.7 million of nonrecurring legal and accounting costs incurred in 2007 associated with a stock option investigation that was completed in early 2007. In addition, the 2008 period reflects a decrease in stock option expense as well as cost savings from the reduction in our workforce in October 2008.

### *Royalty Expense*

Royalty expense of \$3.4 million for the year ended December 31, 2008 reflects an increase of approximately \$2.8 million from the prior year. The 2008 expense primarily consists of a \$2.5 million obligation to Covidien that was due upon the FDA approval of Vasovist and royalties to Ramot at Tel Aviv University Ltd. resulting from the receipt of milestone payments in 2008 from our collaboration partners.

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 acquired from Ramot, and we are required to make payments to Ramot, as described below, as and when rights to any such drug candidates are ever sublicensed or any such drug candidates are commercialized. In addition, we have used the licensed technology in all of our preclinical-stage programs, and would expect to make payments to Ramot if rights to any drug candidates were ever commercialized from any of these programs.

We also are required to share between 5% and 10% of the consideration we receive, including upfront license fee and milestone payments, from parties to whom we grant sublicenses of rights in the Ramot technology or sublicenses of rights in products identified, characterized or developed with the use of such technology and between 2% and 4% of consideration we receive from performing services using such technology. We would also be required to pay Ramot royalties on sales of products developed with the use of such technology.

### *Restructuring Expense*

Restructuring costs amounted to \$0.2 million and \$0.4 million for the years ended December 31, 2008 and 2007, respectively. In October 2008, we eliminated approximately 23% of our workforce in connection

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with our efforts to reduce our cost structure and narrow the focus of our research and development efforts. The charge consisted primarily of severance and related costs.

Restructuring costs for the year ended December 31, 2007 include a restructuring charge of \$0.5 million recorded in the second quarter for the consolidation of a leased laboratory in Cambridge, Massachusetts into our Lexington, Massachusetts facility. The charge consisted primarily of future lease costs through the end of 2007. The consolidation was completed during the second quarter of 2007. In addition, during the second quarter of 2007, we recorded a reduction of our 2006 restructuring charge in the amount of \$0.1 million resulting from a reduction in the amount of space leased at our former headquarters location in Cambridge, Massachusetts.

*Interest and Other Income*

Interest and other income of \$1.4 million for the year ended December 31, 2008 represents a decrease of 72% from 2007. The decrease in interest income in 2008 was primarily due to lower levels of cash and investments available to invest due to cash being used to fund operations as well as lower rates of interest earned on investments during 2008. The 2007 period also included \$0.6 million of income from the settlement of a contract dispute.

*Interest Expense*

Interest expense of \$3.8 million for the year ended December 31, 2008 represents a decrease of 7% from 2007. The decrease in interest expense in 2008 was primarily due to interest incurred in 2007 on the milestone payable to the former shareholders of Predix. The milestone was paid in October 2007.

*Provision for Income Taxes*

The provision for income taxes represents income taxes required to be withheld in Italy on Bracco royalties for MultiHance sales. Royalties on these sales were discontinued in the second quarter of 2007.

*Years ended December 31, 2007 and 2006**Revenue*

The following table presents revenue and revenue growth (decline) for the years ended December 31, 2007 and 2006:

	<b>2007</b>		<b>2006</b>
	<b>Revenue</b>	<b>Increase (Decrease)</b>	<b>Revenue</b>
Product development revenue	\$ 10,239,120	252%	\$ 2,909,402
Royalty revenue	1,017,669	(37)%	1,603,230
License fee revenue	3,703,260	142%	1,527,910
Total	\$ 14,960,049	148%	\$ 6,040,542

Product development revenue increased 252% in the year ended December 31, 2007 compared to the prior year primarily as a result of \$7.8 million of milestones achieved from our collaboration agreements with GlaxoSmithKline and CFFT, as well as revenue from reimbursed research costs earned under both of these agreements. The increases in

revenue for 2007 was partially offset by decreases in revenue due to the completion of our early-stage imaging research programs with Bayer Schering in 2006, as well as lower development revenue for Vasovist.

The decrease in royalty revenue of 37% in the year ended December 31, 2007 compared to the prior year was primarily due to a reduction in royalties on sales of MultiHance by Bracco due to the expiration of patents. Future royalty revenue will consist solely of royalties on sales of Vasovist outside of the United States and Primovist, which are not expected to be significant. We will stop receiving royalties on Vasovist sales effective upon the termination of our collaboration agreement with Bayer Schering on March 1, 2009.

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License fee revenue increased 142% in the year ended December 31, 2007 compared to the prior year primarily as a result of an increase of \$2.5 million in the recognition of deferred revenue from the Amgen and GlaxoSmithKline collaboration agreements. Partially offsetting this increase was a decrease in revenue of \$0.2 million from the recognition of the Bracco license fee as this fee was fully recognized by June 2006. The deferred revenue from our Amgen agreement was fully recognized in October 2007 when our research obligation ended.

### *Research and Development Expense*

Research and development expense of \$57.5 million for the year ended December 31, 2007 reflects an increase of 119% from the prior year. The increase in research and development expense during 2007 was primarily due to an increase in third-party expenses associated with our clinical development programs of \$19.7 million during the twelve months ended December 31, 2007, as well as increased costs for the preclinical programs and internal costs which began after the Predix acquisition was completed on August 16, 2006. Clinical program costs incurred in the current year include costs for the Phase 2b clinical trial of PRX-00023 for depression, costs incurred for the recently completed Phase 2a clinical trial of PRX-03140 for the treatment of Alzheimer's disease, costs incurred for the completed Phase 2a clinical trial of PRX-08066 for the treatment of pulmonary hypertension in association with chronic obstructive pulmonary disease, and costs incurred for the completed Phase 1b multiple ascending dose clinical trials of PRX-07034 for the treatment of obesity and cognitive impairment. The increased costs as described above were partially offset by the discontinuation of spending on imaging programs subsequent to the merger with Predix. Spending during 2007 and 2006 for Vasovist primarily involved costs related to our appeal to the FDA and was not significant.

### *In-Process Research and Development Charge*

In connection with our acquisition of Predix in August of 2006, we incurred a nonrecurring charge of \$123.5 million for in-process research and development. The in-process research and development charge represented the fair value of purchased in-process technology of Predix for research projects that, as of the closing date of the merger, had not reached technological feasibility and have no alternative future use. The in-process research and development primarily represents the fair value of the following drug candidates: PRX-00023 (\$70.9 million) that, as of the date of the merger, was in a Phase 3 clinical trial for the treatment of generalized anxiety disorder; PRX-03140 (\$23.5 million) that, as of the date of the merger had completed Phase 1 clinical trials for the treatment of Alzheimer's disease; PRX-08066 (\$20.2 million) that, as of the date of the merger, had entered a Phase 2 clinical trial for the treatment of pulmonary hypertension in association with COPD; and PRX-07034 (\$8.9 million) that, as of the date of the merger, had entered a Phase 1 clinical trial.

### *General and Administrative Expense*

General and administrative expense of \$20.1 million for the year ended December 31, 2007 reflects an increase of 64% from the prior year. The increase in general and administrative expense during 2007 includes incremental costs associated with the increase in personnel and infrastructure relating to the Predix business that was acquired on August 16, 2006 and higher legal expenses for patent-related matters and general corporate items due to the increased complexity of the post-merger entity. In addition, 2007 includes nonrecurring legal and accounting costs of approximately \$5.7 million associated with our stock option investigation that was completed in the first quarter of 2007.

### *Royalty Expense*

Royalty expense of \$0.6 million for the year ended December 31, 2007 reflects a decrease of approximately \$0.5 million from the prior year. The 2007 expense primarily consists of royalty payments made to Ramot at Tel Aviv

University Ltd. resulting from the receipt of milestone payments in 2007 from our collaboration partners. The 2006 expense primarily consists of the royalty payment to Ramot resulting from the payments we received from the execution of the GlaxoSmithKline agreement in December 2006.

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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 acquired from Ramot, and we are required to make payments to Ramot, as described below, as and when rights to any such drug candidates are ever sublicensed or any such drug candidates are commercialized. In addition, we have used the licensed technology in all of our preclinical-stage programs, and would expect to make payments to Ramot if rights to any drug candidates were ever commercialized from any of these programs.

We also are required to share between 5% and 10% of the consideration we receive, including upfront license fee and milestone payments, from parties to whom we grant sublicenses of rights in the Ramot technology or sublicenses of rights in products identified, characterized or developed with the use of such technology and between 2% and 4% of consideration we receive from performing services using such technology. We would also be required to pay Ramot royalties on sales of products developed with the use of such technology.

### *Restructuring Costs*

Restructuring costs amounted to \$0.4 million and \$0.6 million for the years ended December 31, 2007 and 2006, respectively. Restructuring costs for the twelve months ended December 31, 2007 include a restructuring charge of \$0.5 million recorded in the second quarter for the consolidation of a leased laboratory facility in Cambridge, Massachusetts into our Lexington, Massachusetts facility. The charge consisted primarily of future lease costs through the end of 2007. The consolidation was completed during the second quarter of 2007. In addition, during the second quarter of 2007, we recorded a reduction of our 2006 restructuring charge in the amount of \$0.1 million resulting from a reduction in the amount of space leased at our former headquarters location in Cambridge, Massachusetts.

Restructuring costs of \$0.6 million for the year ended December 31, 2006 include a charge of \$0.2 million recorded in the third quarter for the consolidation of our former Cambridge, Massachusetts headquarters into our Lexington, Massachusetts facility. The charge primarily consists of future lease payments through the end of 2007 and the write-off of leasehold improvements. In addition, in the first quarter of 2006, we recorded a charge of \$0.4 million that represented additional costs related to the December 2005 restructuring whereby we reduced our workforce by 48 employees, or approximately 50%, in response to the FDA's second approvable letter regarding Vasovist. The reductions, which were completed in January 2006, affected both the research and development and the general and administrative areas of the company and included severance costs as well as costs related to vacating certain leased space and the write-off of leasehold improvements.

### *Interest and Other Income*

Interest and other income of \$4.9 million for the year ended December 31, 2007 represents a decrease of 11% from 2006. The decrease in interest income was primarily due to lower levels of cash and investments available to invest due to cash being used to fund operations, partially offset by \$0.6 million received in 2007 from the settlement of a contract dispute.

### *Interest Expense*

Interest expense of \$4.1 million for the year ended December 31, 2007 represents a decrease of 20% from 2006. The decrease in interest expense is primarily due to a \$0.8 million decrease in the value of the embedded derivative relating to the stock portion of the milestone payable to the former shareholders of Predix, partially offset by increased interest expense relating to the cash portion of the milestone payment. Prior to the payment of the milestone to the former shareholders of Predix in October 2007, we recorded interest expense on the milestone at the greater of the stated rate of 10% or the value of the embedded derivative included in the milestone, which provided for the milestone payment to be paid in shares of our common stock based on 75% of the 30-day average closing price of our common



stock ending on October 19, 2007. This embedded derivative was recorded at its fair value and changes in the fair value were recorded as interest expense.

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*Provision for Income Taxes*

The provision for income taxes represents income taxes required to be withheld in Italy on Bracco royalties for MultiHance sales. Royalties on these sales were discontinued in the second quarter of 2007.

**Liquidity and Capital Resources**

Our principal sources of liquidity consist of cash, cash equivalents and available-for-sale marketable securities of \$24.6 million at December 31, 2008 as compared to \$61.1 million at December 31, 2007. The decrease in cash, cash equivalents and available-for-sale marketable securities of \$36.5 million was primarily attributable to funding of ongoing operations during the fiscal year.

We used approximately \$36.4 million of cash to fund operating activities for the year ended December 31, 2008, as compared to a use of \$57.1 million for the same period in 2007. The decrease in the cash used for operating activities in 2008 of \$20.7 million was primarily due to a decrease in the net loss in 2008 of \$26.1 million. The net use of cash to fund operations for the year ended December 31, 2008 primarily resulted from the net loss of \$36.7 million. Working capital changes during 2008 included an increase in accounts receivable of approximately \$1.1 million due to increased activity with our collaboration partners as well as a decrease in contract advances of approximately \$1.0 million due to our spending on the Vasovist reread and NDA resubmission. The net use of cash to fund operations for the year ended December 31, 2007 primarily resulted from the net loss of \$62.8 million, which was partially offset by an increase of \$2.0 million in accounts payable and accrued expenses largely resulting from increased clinical activity at year end. During the year ended December 31, 2007, we also received approximately \$3.3 million of landlord allowances related to the laboratory construction at our Lexington, Massachusetts facility.

Our investing activities provided \$51.8 million of cash during the year ended December 31, 2008 as compared to \$20.5 million of cash during the same period in 2007. Investing activities in 2008 primarily consisted of the net redemption of \$52.5 million of marketable securities to fund operating activities partially offset by \$0.8 million of capital expenditures. Investing activities in 2007 primarily consisted of the net redemption of \$29.6 million of marketable securities to fund operating activities, \$4.2 million of capital expenditures primarily related to the build out of laboratory space at our Lexington facility and \$5.3 million for the cash payment of the principal portion of the second milestone for the Predix merger.

Our financing activities provided \$0.1 million of cash during the year ended December 31, 2008 primarily due to \$0.3 million received from the issuance of common stock and \$0.2 million of capital lease payments. Our financing activities provided \$15.5 million of cash during the year ended December 31, 2007, primarily due to \$15.0 million of proceeds received from the private placement of our common stock in November 2007.

Our primary sources of cash include quarterly payments from CFFT and GlaxoSmithKline for research services. Other potential cash inflows include future milestone and option payments from our current strategic collaborators, GlaxoSmithKline, Amgen, and CFFT. Because of anticipated spending for the continued development of our preclinical and clinical compounds, we do not expect positive cash flow from operating activities for at least the next several years. Known outflows, in addition to our ongoing research and development and general and administrative expenses, include interest on our \$100.0 million convertible notes at a rate of 3% payable semi-annually on June 15 and December 15.

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The following table represents payments due under contractual obligations as of December 31, 2008:

Contractual Obligations	Total	Payments Due by Period			
		Less Than 1 Year	1-3 Years	3-5 Years	More Than 5 Years
Long-term debt obligations, including interest payments	\$ 107,500,000	\$ 3,000,000	\$ 104,500,000	\$	\$
Operating lease obligations	12,852,415	2,686,070	4,647,960	3,648,625	1,869,760
Capital lease obligations	475,382	250,113	225,269		
Unconditional purchase obligations	1,090,107	1,090,107			
Other long-term liabilities	2,905,000	525,000	280,000	280,000	1,820,000
<b>Total</b>	<b>\$ 124,822,904</b>	<b>\$ 7,551,290</b>	<b>\$ 109,653,229</b>	<b>\$ 3,928,625</b>	<b>\$ 3,689,760</b>

On February 4, 2009, we received notice from the Listing Qualifications Panel of the NASDAQ Stock Market LLC, or NASDAQ, that it has determined to continue the listing of our common stock on the NASDAQ Global Market subject to our compliance with Marketplace Rule 4450(b)(1)(A), which requires us to maintain a market value of our common stock of at least \$50,000,000 for at least 10 consecutive days on or prior to May 11, 2009. As of March 10, 2009, we were not in compliance with the requirement for continued inclusion on NASDAQ. If we do not regain compliance with the rules for continued listing on NASDAQ, our common stock will be delisted from NASDAQ. If our common stock is delisted from NASDAQ, the holders of our \$100 million aggregate principal amount of 3% Convertible Senior Notes could redeem their notes at face value, plus accrued and unpaid interest. We currently do not have sufficient funds to repurchase more than a nominal amount of the notes if tendered by the holders. Accordingly, we will need to raise significant additional capital to fund our operations beyond August 2009 or if we are required to redeem the notes. If we are unable to obtain such additional capital, we will not be able to sustain our operations and would be required to cease our operations and/or seek bankruptcy protection.

We estimate that cash and cash equivalents on hand as of December 31, 2008 and anticipated revenue we will earn in the first half of 2009 cannot fund our operations beyond August 2009. This projection is based on our current cost structure and our current expectations regarding operating expenses and anticipated revenues. Although we are eligible for milestone payments and/or royalty payments under our agreements with GlaxoSmithKline, Amgen and CFFT, we do not expect any such payments will materially supplement our liquidity position to extend our available cash beyond the end of August 2009. As a result of our recurring operating losses and need for additional financing, the audit report relating to our consolidated financial statements for the year ended December 31, 2008 contains an explanatory paragraph regarding our ability to continue as a going concern. We will need to raise additional capital prior to the end of August 2009 to continue our current operations beyond the end of the August 2009. If we are unable to obtain additional capital prior to the end of August 2009, or sooner if our common stock is delisted from the NASDAQ Stock Market and holders of our 3% Convertible Senior Notes require redemption of the notes, we will not be able to sustain our operations and would be required to cease our operations and/or seek bankruptcy protection.

Given the difficult current economic environment, we believe that it will be difficult for companies such as ours to raise additional funds and there can be no assurance as to the availability of additional financing or the terms upon which additional financing may be available. If we are able to raise sufficient additional capital prior to the end of August 2009 to continue our current operations, our future liquidity and additional capital requirements will depend on numerous factors, including the following: the progress and scope of clinical and preclinical 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 products, if any, gain market acceptance; the timing and costs of product introductions; the extent of our ongoing and new research and development programs; the costs of training physicians to become proficient with the use of our potential products; and, if necessary, once regulatory approvals are received, the costs of developing marketing and distribution capabilities. In addition, if holders of our convertible senior notes require redemption of the notes,

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we would be required to repay \$100.0 million, 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 or termination of trading of our common stock on the NASDAQ Stock Market.

On August 4, 2008, we entered into a Committed Equity Financing Facility (CEFF) with Kingsbridge Capital Limited or Kingsbridge, pursuant to which Kingsbridge committed to purchase, subject to certain conditions, up to the lesser of approximately 8.3 million shares of our common stock or an aggregate of \$50.0 million of our common stock during the next three years. In September 2008, we drew down on the CEFF and issued 94,627 shares of our common stock, \$0.01 par value per share, to Kingsbridge at an aggregate purchase price of \$113,750. Kingsbridge is not obligated to purchase shares at prices below \$1.25 per share or if the volume-weighted average price of our common stock is below 90% of the closing market value of our common stock on the trading day immediately preceding the commencement of the drawdown. We did not receive any additional proceeds from drawdowns subsequent to September 2008 and based on our stock price of \$0.48 on March 10, 2009, we are not currently able to sell shares under the CEFF and will continue to be restricted from any drawdown unless the trading price of our common stock reaches at least \$1.25.

**ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK**

The objective of our investment activities is to preserve principal, while at the same time maximizing yields without significantly increasing risk. To achieve this objective, in accordance with our investment policy, we invest our cash in a variety of financial instruments, principally restricted to government-sponsored enterprises, high-grade bank obligations, high-grade corporate bonds, high-grade asset-backed securities, and certain money market funds. These investments are denominated in U.S. dollars.

Investments in both fixed rate and floating rate interest earning instruments carry a degree of interest rate risk. Fixed rate securities may have their fair market value adversely impacted due to a rise in interest rates, while floating rate securities may produce less income than expected if interest rates fall. Due in part to these factors, our future investment income may fall short of expectations due to changes in interest rates or we may suffer losses in principal if forced to sell securities that have seen a decline in market value due to changes in interest rates. A hypothetical 10% increase or decrease in interest rates would result in an insignificant change in the fair market value of our total portfolio at December 31, 2008.

**ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA**

<b>Index to Consolidated Financial Statements</b>	<b>Number</b>
Report of Independent Registered Public Accounting Firm	F-2
Consolidated Financial Statements:	
Consolidated Balance Sheets	F-3
Consolidated Statements of Operations	F-4
Consolidated Statements of Stockholders' Equity (Deficit)	F-5
Consolidated Statements of Cash Flows	F-6
Notes to Consolidated Financial Statements	F-7

**ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE**

There have been no disagreements with accountants on accounting or financial disclosure matters during our two most recent fiscal years.

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**Item 9A. CONTROLS AND PROCEDURES**

**Management's Evaluation of Disclosure Controls and Procedures**

Our management, with the participation of our chief executive officer and chief financial officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e)) as of December 31, 2008. Based on this evaluation, our chief executive officer and chief financial officer concluded that, as of December 31, 2008, our disclosure controls and procedures were effective in providing reasonable assurance that information required to be disclosed by us in reports that we file or submit under the Exchange Act is recorded, processed, summarized, reported and accumulated and communicated to our management, including our chief executive officer and chief financial officer, as appropriate to allow timely decisions regarding required disclosure.

**Management's Annual Report on Internal Control Over Financial Reporting**

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) under the Securities Exchange Act of 1934, as amended, as a process designed by, or under the supervision of, our principal executive and principal financial officers and effected by our board of directors, management and other personnel to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Our internal control over financial reporting includes those policies and procedures that:

- pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflects transactions in and dispositions of our assets;

- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and

- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

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

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2008. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework.

Based on our assessment, management concludes that, as of December 31, 2008, our internal control over financial reporting is effective based on those criteria.

The company's independent registered public accounting firm, Ernst & Young LLP, has audited the effectiveness of the company's internal control over financial reporting as of December 31, 2008, as stated in their report that appears on page 60 of this Annual Report on Form 10-K.

**Changes in Internal Controls over Financial Reporting**

There was no change in our internal control over financial reporting that occurred during the fourth quarter of 2008 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

**Item 9B. *OTHER INFORMATION***

None.



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**Report of Independent Registered Public Accounting Firm**

The Board of Directors and Stockholders of  
EPIX Pharmaceuticals, Inc.

We have audited EPIX Pharmaceuticals Inc.'s internal control over financial reporting as of December 31, 2008, based on criteria established in Internal Control – Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). EPIX Pharmaceuticals, Inc.'s management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Controls. Our responsibility is to express an opinion on the company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

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

In our opinion, EPIX Pharmaceuticals Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2008, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of EPIX Pharmaceuticals, Inc. as of December 31, 2008 and 2007, and the related consolidated statements of operations, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2008 of EPIX Pharmaceuticals, Inc. and our report dated March 11, 2009 expressed an unqualified opinion thereon that included an explanatory paragraph regarding EPIX Pharmaceuticals, Inc.'s ability to continue as a going concern.

/s/ Ernst & Young LLP

Boston, Massachusetts  
March 11, 2009

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**PART III**

**ITEM 10. *DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE***

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2008.

**ITEM 11. *EXECUTIVE COMPENSATION***

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2008.

**ITEM 12. *SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS***

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2008.

**ITEM 13. *CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE***

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2008.

**ITEM 14. *PRINCIPAL ACCOUNTING FEES AND SERVICES***

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2008.

**PART IV**

**ITEM 15. *EXHIBITS, FINANCIAL STATEMENT SCHEDULES***

**Item 15(a).**

The following documents are filed as part of this Annual Report on Form 10-K

**Item 15(a) (1) and (2).**

See "Index to Financial Statements" at Item 8 to this Annual Report on Form 10-K. Financial statement schedules have not been included because they are not applicable or the information is included in the financial statements or notes thereto.



**Table of Contents****Item 15(a) (3). Exhibits**

The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

<b>Exhibit Number</b>	<b>Description</b>
3.1@	Restated Certificate of Incorporation of the Company. Filed as Exhibit 3.1 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
3.2@	Amended and Restated By-Laws of the Company. Filed as Exhibit 3.1 to the Company's Quarterly Report on Form 10-Q for the period ended March 31, 2007 and incorporated herein by reference.
4.1@	Specimen certificate for shares of Common Stock of the Company. Filed as Exhibit 4.1 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
4.2@	Indenture dated as of June 7, 2004 between the Company and U.S. Bank National Association as Trustee, relating to 3% Convertible Senior Notes due June 15, 2024. Filed as Exhibit 4.1 to the Company's Current Report on Form 8-K filed June 7, 2004 and incorporated herein by reference.
4.3@	Warrant issued to RRD International, LLC. Filed as Exhibit 4.3 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
4.4@	Warrant issued to General Electric Capital Corporation. Filed as Exhibit 4.4 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
4.5@	Warrant issued to Kingsbridge Capital Limited, dated as of August 4, 2008. Filed as Exhibit 4.1 to the Company's Current Report on Form 8-K filed August 5, 2008 and incorporated herein by reference.
10.1@+	Amended and Restated License Agreement between the Company and The General Hospital Corporation dated July 10, 1995. Filed as Exhibit 10.14 to the Company's Registration Statement on Form S-1 filed December 10, 1996 (File No. 333-17581) and incorporated herein by reference.
10.2@#	Amended and Restated 1992 Incentive Plan. Filed as Appendix A to the Company's 2005 Definitive Proxy Statement on Schedule 14A filed April 29, 2005 and incorporated herein by reference.
10.3@#	Form of Incentive Stock Option Certificate under the Amended and Restated 1992 Incentive Plan. Filed as Exhibit 10.29 to the Company's Registration Statement on Form S-1 filed December 10, 1996 (File No. 333-17581) and incorporated herein by reference.
10.4@#	Form of Nonstatutory Stock Option Certificate under the Amended and Restated 1992 Incentive Plan. Filed as Exhibit 10.30 to the Company's Registration Statement on Form S-1 filed December 10, 1996 (File No. 333-17581) and incorporated herein by reference.
10.5@#	Amended and Restated 1996 Director Stock Option Plan. Filed as Appendix B to the Company's 2005 Definitive Proxy Statement on Schedule 14A filed April 29, 2005 and incorporated herein by reference.
10.6@++	Amended and Restated Strategic Collaboration Agreement dated as of June 9, 2000, among the Company, Mallinckrodt Inc. (a Delaware corporation) and Mallinckrodt Inc. (a New York corporation). Filed as Exhibit 10.6 to the Company's Annual Report on Form 10-K for the year ended December 31, 2007 and incorporated herein by reference.
10.7@++	Strategic Collaboration Agreement dated as of June 9, 2000, between the Company and Schering Aktiengesellschaft. Filed as Exhibit 10.7 to the Company's Annual Report on Form 10-K for the year ended December 31, 2007 and incorporated herein by reference.
10.8@	Amendment No. 1 dated as of December 22, 2000 to the Strategic Collaboration Agreement, dated as of June 9, 2000, between the Company and Schering Aktiengesellschaft. Filed as Exhibit 10.8 to the Company's Annual Report on Form 10-K for the year ended December 31, 2007 and incorporated herein by reference.



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<b>Exhibit Number</b>	<b>Description</b>
10.9*	Intellectual Property Agreement by and between the Company and Dr. Martin R. Prince, dated November 17, 2003.
10.10@#	Description of Director Compensation Arrangements. Filed with the Company's Current Report on Form 8-K filed June 4, 2007 and incorporated herein by reference.
10.11@#	Form of Indemnification Agreement. Filed as Exhibit 10.29 to the Company's Annual Report on Form 10-K for the year ended December 31, 2004 and incorporated herein by reference.
10.12@	Form of Amendment to Stock Option Agreement under the Amended and Restated 1992 Incentive Plan. Filed as Exhibit 10.30 to the Company's Annual Report on Form 10-K for the year ended December 31, 2004 and incorporated herein by reference.
10.13@	Predix Pharmaceuticals Holdings, Inc. Amended and Restated 2003 Stock Incentive Plan. Filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.14@	Physiome Sciences, Inc. Stock Option Plan (as amended September 21, 2001). Filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.15@++	Amended and Restated License Agreement between Ramot at Tel Aviv University Ltd., Company Registration No. 51-066714-0 and Predix Pharmaceuticals Holdings, Inc., dated as of May 20, 2004. Filed as Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.16@++	Research, Development and Commercialization Agreement between Predix Pharmaceuticals Holdings, Inc. and Cystic Fibrosis Foundation Therapeutics, Incorporated, dated as of March 7, 2005. Filed as Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.17@++	License Agreement between Amgen Inc. and Predix Pharmaceuticals Holdings, Inc., dated as of July 31, 2006. Filed as Exhibit 10.5 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.18@	Lease between Trustees of 4 Maguire Road Realty Trust and EPIX Delaware, Inc. dated as of January 30, 1998, as amended through June 2, 2008. Filed as Exhibit 10.6 to the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2008 and incorporated herein by reference.
10.19@	Lease Agreement by and between 150 College Road, LLC and Physiome Sciences, Inc., dated as of December 21, 2000, as amended. Filed as Exhibit 10.7 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.20@	Sublease by and between Predix Pharmaceuticals Holdings, Inc. and Novo Nordisk Pharmaceuticals, Inc., dated as of December 12, 2003. Filed as Exhibit 10.8 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.21@	Unprotected Lease Agreement between Emed Real Estate Development and Investments Company Ltd. and Predix Pharmaceuticals Ltd., dated as of September 26, 2004. Filed as Exhibit 10.9 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.22@++	Development and License Agreement among SmithKline Beecham Corporation, doing business as GlaxoSmithKline, Glaxo Group Limited and the Company, dated as of December 11, 2006. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K/A filed January 18, 2007 and incorporated herein by reference.
10.23@	Stock Purchase Agreement among the Company, Glaxo Group Limited and SmithKline Beecham Corporation, doing business as GlaxoSmithKline, dated as of December 11, 2006. Filed as Exhibit 10.2

to the Company's Current Report on Form 8-K/A filed January 18, 2007 and incorporated herein by reference.



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<b>Exhibit Number</b>	<b>Description</b>
10.24@	First Amendment to License Agreement between Amgen Inc. and the Company, dated as of March 20, 2007. Filed as Exhibit 10.52 to the Company's Annual Report on Form 10-K for the year ended December 31, 2006 and incorporated herein by reference.
10.25@#	Employment Agreement between the Company and Michael G. Kauffman, M.D., Ph.D., dated as of March 27, 2007. Filed as Exhibit 10.2 to the Company's Current Report on Form 8-K filed March 29, 2007 and incorporated herein by reference.
10.26@#	2006 Employee Stock Purchase Plan. Filed as Appendix A to the Company's 2007 Definitive Proxy Statement on Schedule 14A filed April 30, 2007 and incorporated herein by reference.
10.27@++	First Amendment to Amended and Restated License Agreement between the Company and Ramot at Tel Aviv University Ltd., dated as of June 13, 2007. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed June 15, 2007 and incorporated herein by reference.
10.28@#	Employment Agreement between the Company and Andrew Uprichard, MD, dated as of August 9, 2007. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed August 10, 2007 and incorporated herein by reference.
10.29@++	Third Amendment to Research, Development and Commercialization Agreement between the Company and Cystic Fibrosis Foundation Therapeutics, Incorporated, dated as of November 1, 2007. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed November 7, 2007 and incorporated herein by reference.
10.30@	Form of Securities Purchase Agreement dated November 9, 2007 between the Company and each of the purchasers listed on Exhibit A thereto. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed November 15, 2007 and incorporated herein by reference.
10.31@#	Form of Restricted Stock Unit Agreement under the Amended and Restated 1992 Incentive Plan. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed February 22, 2008 and incorporated herein by reference.
10.32@#	Form of Restricted Stock Unit Agreement under the Amended and Restated 2003 Stock Option and Incentive Plan. Filed as Exhibit 10.2 to the Company's Current Report on Form 8-K filed February 22, 2008 and incorporated herein by reference.
10.33@++	Research, Development and Commercialization Agreement between EPIX Pharmaceuticals, Inc. and Cystic Fibrosis Foundation Therapeutics, Inc., dated as of April 1, 2008. Filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the period ended March 31, 2008 and incorporated herein by reference.
10.34@#	Letter Agreement between the Company and Elkan Gamzu, Ph.D., dated as of July 25, 2008. Filed as Exhibit 10.2 to the Company's Current Report on Form 8-K filed July 28, 2008 and incorporated herein by reference.
10.35@#	Employment Agreement between the Company and Chen Schor, dated as of June 16, 2008. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed June 19, 2008 and incorporated herein by reference.
10.36@#	Separation Agreement and Post-Employment Consulting Agreement between the Company and Andrew Uprichard, M.D., dated May 29, 2008. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed June 3, 2008 and incorporated herein by reference.
10.37@#	Separation Agreement between the Company and Michael G. Kauffman, M.D., Ph.D., dated as of July 25, 2008. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed July 28, 2008 and incorporated herein by reference.
10.38@#	2008 Stock Option and Incentive Plan and forms of award agreements thereunder. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed May 21, 2008 and incorporated herein by reference.

10.39@# Employment Agreement between the Company and Kim C. Drapkin, dated as of September 15, 2008. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed September 18, 2008 and incorporated herein by reference.

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<b>Exhibit Number</b>	<b>Description</b>
10.40@#	Amendment to Employment Agreement between the Company and Chen Schor, dated as of September 16, 2008. Filed as Exhibit 10.2 to the Company's Current Report on Form 8-K filed September 18, 2008 and incorporated herein by reference.
10.41@	Common Stock Purchase Agreement between the Company and Kingsbridge Capital Limited, dated as of August 4, 2008. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed August 5, 2008 and incorporated herein by reference.
10.42@	Registration Rights Agreement between the Company and Kingsbridge Capital Limited, dated as of August 4, 2008. Filed as Exhibit 10.2 to the Company's Current Report on Form 8-K filed August 5, 2008 and incorporated herein by reference.
12.1*	Ratio of Earnings to Fixed Charges.
21.1@	Subsidiaries of the Company. Filed as Exhibit 21.1 to the Company's Annual Report on Form 10-K for the year ended December 31, 2006 and incorporated herein by reference.
23.1*	Consent of Independent Registered Public Accounting Firm.
24.1	Power of Attorney (included on signature page to this Annual Report on Form 10-K).
31.1*	Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 for Elkan Gamzu, Ph.D.
31.2*	Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 for Kim Cobleigh Drapkin.
32*	Certification pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (Subsections (a) and (b) of Section 1350, Chapter 63 of Title 18, U.S. Code).

@ Incorporated by reference as indicated.

\* Filed herewith.

# Identifies a management contract or compensatory plan or agreement in which an executive officer or director of the Company participates.

+ Certain confidential material contained in the document has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

++ Certain confidential material contained in the document has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

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**SIGNATURES**

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

EPIX PHARMACEUTICALS, INC.

By: /s/ KIM COBLEIGH DRAPKIN

Kim Cobleigh Drapkin, CPA  
 Chief Financial Officer  
 (Principal Financial and Accounting Officer)

March 13, 2009

**POWER OF ATTORNEY**

KNOW ALL MEN BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Elkan Gamzu, Ph.D. and Kim Cobleigh Drapkin, CPA, jointly and severally, his or her attorney-in-fact, with the power of substitution, for him or her in any and all capacities, to sign any amendments to this Annual Report on Form 10-K and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact, or his or her substitute or substitutes, may do or cause to be done by virtue hereof.

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

<b>Signature</b>	<b>Title</b>	<b>Date</b>
/s/ ELKAN GAMZU Elkan Gamzu, Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	March 13, 2009
/s/ KIM COBLEIGH DRAPKIN Kim Cobleigh Drapkin, CPA	Chief Financial Officer (Principal Financial and Accounting Officer)	March 13, 2009
/s/ FREDERICK FRANK Frederick Frank	Chairman of the Board of Directors	March 13, 2009
/s/ MICHAEL GILMAN Michael Gilman, Ph.D.	Director	March 13, 2009
/s/ MARK LEUCHTENBERGER Mark Leuchtenberger	Director	March 13, 2009

/s/ GREGORY D. PHELPS

Director

March 13, 2009

Gregory D. Phelps

/s/ IAN F. SMITH

Director

March 13, 2009

Ian F. Smith, CPA, ACA

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

<b>Exhibit Number</b>	<b>Description</b>
3.1@	Restated Certificate of Incorporation of the Company. Filed as Exhibit 3.1 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
3.2@	Amended and Restated By-Laws of the Company. Filed as Exhibit 3.1 to the Company's Quarterly Report on Form 10-Q for the period ended March 31, 2007 and incorporated herein by reference.
4.1@	Specimen certificate for shares of Common Stock of the Company. Filed as Exhibit 4.1 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
4.2@	Indenture dated as of June 7, 2004 between the Company and U.S. Bank National Association as Trustee, relating to 3% Convertible Senior Notes due June 15, 2024. Filed as Exhibit 4.1 to the Company's Current Report on Form 8-K filed June 7, 2004 and incorporated herein by reference.
4.3@	Warrant issued to RRD International, LLC. Filed as Exhibit 4.3 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
4.4@	Warrant issued to General Electric Capital Corporation. Filed as Exhibit 4.4 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
4.5@	Warrant issued to Kingsbridge Capital Limited, dated as of August 4, 2008. Filed as Exhibit 4.1 to the Company's Current Report on Form 8-K filed August 5, 2008 and incorporated herein by reference.
10.1@+	Amended and Restated License Agreement between the Company and The General Hospital Corporation dated July 10, 1995. Filed as Exhibit 10.14 to the Company's Registration Statement on Form S-1 filed December 10, 1996 (File No. 333-17581) and incorporated herein by reference.
10.2@#	Amended and Restated 1992 Incentive Plan. Filed as Appendix A to the Company's 2005 Definitive Proxy Statement on Schedule 14A filed April 29, 2005 and incorporated herein by reference.
10.3@#	Form of Incentive Stock Option Certificate under the Amended and Restated 1992 Incentive Plan. Filed as Exhibit 10.29 to the Company's Registration Statement on Form S-1 filed December 10, 1996 (File No. 333-17581) and incorporated herein by reference.
10.4@#	Form of Nonstatutory Stock Option Certificate under the Amended and Restated 1992 Incentive Plan. Filed as Exhibit 10.30 to the Company's Registration Statement on Form S-1 filed December 10, 1996 (File No. 333-17581) and incorporated herein by reference.
10.5@#	Amended and Restated 1996 Director Stock Option Plan. Filed as Appendix B to the Company's 2005 Definitive Proxy Statement on Schedule 14A filed April 29, 2005 and incorporated herein by reference.
10.6@++	Amended and Restated Strategic Collaboration Agreement dated as of June 9, 2000, among the Company, Mallinckrodt Inc. (a Delaware corporation) and Mallinckrodt Inc. (a New York corporation). Filed as Exhibit 10.6 to the Company's Annual Report on Form 10-K for the year ended December 31, 2007 and incorporated herein by reference.
10.7@++	Strategic Collaboration Agreement dated as of June 9, 2000, between the Company and Schering Aktiengesellschaft. Filed as Exhibit 10.7 to the Company's Annual Report on Form 10-K for the year ended December 31, 2007 and incorporated herein by reference.
10.8@	Amendment No. 1 dated as of December 22, 2000 to the Strategic Collaboration Agreement, dated as of June 9, 2000, between the Company and Schering Aktiengesellschaft. Filed as Exhibit 10.8 to the Company's Annual Report on Form 10-K for the year ended December 31, 2007 and incorporated herein by reference.
10.9*	Intellectual Property Agreement by and between the Company and Dr. Martin R. Prince, dated November 17, 2003.
10.10@#	

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

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<b>Exhibit Number</b>	<b>Description</b>
10.11@#	Form of Indemnification Agreement. Filed as Exhibit 10.29 to the Company's Annual Report on Form 10-K for the year ended December 31, 2004 and incorporated herein by reference.
10.12@	Form of Amendment to Stock Option Agreement under the Amended and Restated 1992 Incentive Plan. Filed as Exhibit 10.30 to the Company's Annual Report on Form 10-K for the year ended December 31, 2004 and incorporated herein by reference.
10.13@	Predix Pharmaceuticals Holdings, Inc. Amended and Restated 2003 Stock Incentive Plan. Filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.14@	Physiome Sciences, Inc. Stock Option Plan (as amended September 21, 2001). Filed as Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.15@++	Amended and Restated License Agreement between Ramot at Tel Aviv University Ltd., Company Registration No. 51-066714-0 and Predix Pharmaceuticals Holdings, Inc., dated as of May 20, 2004. Filed as Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.16@++	Research, Development and Commercialization Agreement between Predix Pharmaceuticals Holdings, Inc. and Cystic Fibrosis Foundation Therapeutics, Incorporated, dated as of March 7, 2005. Filed as Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.17@++	License Agreement between Amgen Inc. and Predix Pharmaceuticals Holdings, Inc., dated as of July 31, 2006. Filed as Exhibit 10.5 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.18@	Lease between Trustees of 4 Maguire Road Realty Trust and EPIX Delaware, Inc. dated as of January 30, 1998, as amended through June 2, 2008. Filed as Exhibit 10.6 to the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2008 and incorporated herein by reference.
10.19@	Lease Agreement by and between 150 College Road, LLC and Physiome Sciences, Inc., dated as of December 21, 2000, as amended. Filed as Exhibit 10.7 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.20@	Sublease by and between Predix Pharmaceuticals Holdings, Inc. and Novo Nordisk Pharmaceuticals, Inc., dated as of December 12, 2003. Filed as Exhibit 10.8 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.21@	Unprotected Lease Agreement between Emed Real Estate Development and Investments Company Ltd. and Predix Pharmaceuticals Ltd., dated as of September 26, 2004. Filed as Exhibit 10.9 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.22@++	Development and License Agreement among SmithKline Beecham Corporation, doing business as GlaxoSmithKline, Glaxo Group Limited and the Company, dated as of December 11, 2006. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K/A filed January 18, 2007 and incorporated herein by reference.
10.23@	Stock Purchase Agreement among the Company, Glaxo Group Limited and SmithKline Beecham Corporation, doing business as GlaxoSmithKline, dated as of December 11, 2006. Filed as Exhibit 10.2 to the Company's Current Report on Form 8-K/A filed January 18, 2007 and incorporated herein by reference.
10.24@	First Amendment to License Agreement between Amgen Inc. and the Company, dated as of March 20, 2007. Filed as Exhibit 10.52 to the Company's Annual Report on Form 10-K for the year ended



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December 31, 2006 and incorporated herein by reference.

- 10.25@# Employment Agreement between the Company and Michael G. Kauffman, M.D., Ph.D., dated as of March 27, 2007. Filed as Exhibit 10.2 to the Company's Current Report on Form 8-K filed March 29, 2007 and incorporated herein by reference.
- 10.26@# 2006 Employee Stock Purchase Plan. Filed as Appendix A to the Company's 2007 Definitive Proxy Statement on Schedule 14A filed April 30, 2007 and incorporated herein by reference.

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<b>Exhibit Number</b>	<b>Description</b>
10.27@++	First Amendment to Amended and Restated License Agreement between the Company and Ramot at Tel Aviv University Ltd., dated as of June 13, 2007. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed June 15, 2007 and incorporated herein by reference.
10.28@#	Employment Agreement between the Company and Andrew Uprichard, MD, dated as of August 9, 2007. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed August 10, 2007 and incorporated herein by reference.
10.29@++	Third Amendment to Research, Development and Commercialization Agreement between the Company and Cystic Fibrosis Foundation Therapeutics, Incorporated, dated as of November 1, 2007. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed November 7, 2007 and incorporated herein by reference.
10.30@	Form of Securities Purchase Agreement dated November 9, 2007 between the Company and each of the purchasers listed on Exhibit A thereto. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed November 15, 2007 and incorporated herein by reference.
10.31@#	Form of Restricted Stock Unit Agreement under the Amended and Restated 1992 Incentive Plan. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed February 22, 2008 and incorporated herein by reference.
10.32@#	Form of Restricted Stock Unit Agreement under the Amended and Restated 2003 Stock Option and Incentive Plan. Filed as Exhibit 10.2 to the Company's Current Report on Form 8-K filed February 22, 2008 and incorporated herein by reference.
10.33@++	Research, Development and Commercialization Agreement between EPIX Pharmaceuticals, Inc. and Cystic Fibrosis Foundation Therapeutics, Inc., dated as of April 1, 2008. Filed as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the period ended March 31, 2008 and incorporated herein by reference.
10.34@#	Letter Agreement between the Company and Elkan Gamzu, Ph.D., dated as of July 25, 2008. Filed as Exhibit 10.2 to the Company's Current Report on Form 8-K filed July 28, 2008 and incorporated herein by reference.
10.35@#	Employment Agreement between the Company and Chen Schor, dated as of June 16, 2008. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed June 19, 2008 and incorporated herein by reference.
10.36@#	Separation Agreement and Post-Employment Consulting Agreement between the Company and Andrew Uprichard, M.D., dated May 29, 2008. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed June 3, 2008 and incorporated herein by reference.
10.37@#	Separation Agreement between the Company and Michael G. Kauffman, M.D., Ph.D., dated as of July 25, 2008. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed July 28, 2008 and incorporated herein by reference.
10.38@#	2008 Stock Option and Incentive Plan and forms of award agreements thereunder. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed May 21, 2008 and incorporated herein by reference.
10.39@#	Employment Agreement between the Company and Kim C. Drapkin, dated as of September 15, 2008. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed September 18, 2008 and incorporated herein by reference.
10.40@#	Amendment to Employment Agreement between the Company and Chen Schor, dated as of September 16, 2008. Filed as Exhibit 10.2 to the Company's Current Report on Form 8-K filed September 18, 2008 and incorporated herein by reference.
10.41@	Common Stock Purchase Agreement between the Company and Kingsbridge Capital Limited, dated as of August 4, 2008. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed August 5,

	2008 and incorporated herein by reference.
10.42@	Registration Rights Agreement between the Company and Kingsbridge Capital Limited, dated as of August 4, 2008. Filed as Exhibit 10.2 to the Company's Current Report on Form 8-K filed August 5, 2008 and incorporated herein by reference.
12.1*	Ratio of Earnings to Fixed Charges.

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<b>Exhibit Number</b>	<b>Description</b>
21.1@	Subsidiaries of the Company. Filed as Exhibit 21.1 to the Company's Annual Report on Form 10-K for the year ended December 31, 2006 and incorporated herein by reference.
23.1*	Consent of Independent Registered Public Accounting Firm.
24.1	Power of Attorney (included on signature page to this Annual Report on Form 10-K).
31.1*	Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 for Elkan Gamzu, Ph.D.
31.2*	Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 for Kim Cobleigh Drapkin.
32*	Certification pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (Subsections (a) and (b) of Section 1350, Chapter 63 of Title 18, U.S. Code).

@ Incorporated by reference as indicated.

\* Filed herewith.

# Identifies a management contract or compensatory plan or agreement in which an executive officer or director of the Company participates.

+ Certain confidential material contained in the document has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

++ Certain confidential material contained in the document has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

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**EPIX PHARMACEUTICALS, INC.**

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**REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

The Board of Directors and Stockholders  
EPIX Pharmaceuticals, Inc.

We have audited the accompanying consolidated balance sheets of EPIX Pharmaceuticals, Inc. as of December 31, 2008 and 2007, and the related consolidated statements of operations, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2008. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of EPIX Pharmaceuticals, Inc. at December 31, 2008 and 2007, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2008, in conformity with U.S. generally accepted accounting principles.

The accompanying financial statements have been prepared assuming that EPIX Pharmaceuticals, Inc. will continue as a going concern. As more fully described in Note 1, the Company has incurred recurring operating losses, has a net capital deficiency and does not have sufficient cash to fund operations beyond December 31, 2009. In addition, the Company has until May 11, 2009 under a NASDAQ ruling to maintain its listing. A delisting from NASDAQ would cause a covenant violation of the Company's convertible debenture agreement that would make the convertible notes redeemable. These conditions raise substantial doubt about the Company's ability to continue as a going concern. Management's plans in regard to these matters also are described in Note 1. The 2008 financial statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from the outcome of this uncertainty.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), EPIX Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2008, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 11, 2009 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts  
March 11, 2009

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**EPIX PHARMACEUTICALS, INC.**  
**CONSOLIDATED BALANCE SHEETS**

	<b>December 31,</b>	
	<b>2008</b>	<b>2007</b>
<b>ASSETS</b>		
Current assets:		
Cash and cash equivalents	\$ 24,596,683	\$ 9,157,973
Available-for-sale marketable securities		51,919,128
Accounts receivable	1,752,094	639,396
Prepaid expenses and other assets	1,424,327	1,523,499
 Total current assets	 27,773,104	 63,239,996
Property and equipment, net	5,300,682	6,044,886
Other assets	3,055,859	3,850,431
Goodwill	4,939,814	4,939,814
 Total assets	 \$ 41,069,459	 \$ 78,075,127
<b>LIABILITIES AND STOCKHOLDERS DEFICIT</b>		
Current liabilities:		
Accounts payable	\$ 1,058,563	\$ 3,539,099
Accrued expenses	9,646,509	8,099,539
Contract advances	3,679,287	4,719,201
Current portion of capital lease obligation	221,585	179,859
Current portion of deferred revenue	1,500,412	1,372,042
Other current liabilities	778,136	610,867
 Total current liabilities	 16,884,492	 18,520,607
Deferred revenue	13,791,549	15,688,296
Capital lease obligation	214,143	182,748
Other liabilities	4,270,345	4,975,123
Convertible debt	100,000,000	100,000,000
 Total liabilities	 135,160,529	 139,366,774
Commitments and contingencies (Note 8)		
Stockholders' deficit:		
Preferred Stock, \$0.01 par value, 1,000,000 shares authorized; no shares issued		
Common Stock, \$0.01 par value, 100,000,000 shares authorized; 41,914,691 and 41,353,079 shares issued and outstanding at December 31, 2008 and December 31, 2007, respectively	419,147	413,530
Additional paid-in-capital	350,318,033	346,289,024
Accumulated deficit	(444,828,250)	(408,157,261)
Accumulated other comprehensive income		163,060

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Total stockholders' deficit	(94,091,070)	(61,291,647)
Total liabilities and stockholders' deficit	\$ 41,069,459	\$ 78,075,127

See accompanying notes.

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**Table of Contents****EPIX PHARMACEUTICALS, INC.****CONSOLIDATED STATEMENTS OF OPERATIONS**

	<b>Year Ended December 31,</b>		
	<b>2008</b>	<b>2007</b>	<b>2006</b>
Revenues:			
Product development revenue	\$ 26,190,203	\$ 10,239,120	\$ 2,909,402
Royalty revenue	626,228	1,017,669	1,603,230
License fee revenue	1,811,924	3,703,260	1,527,910
Total revenues	28,628,355	14,960,049	6,040,542
Operating expenses:			
Research and development	46,241,139	57,526,506	26,255,000
Acquired in-process research and development			123,500,000
General and administrative	13,023,701	20,051,893	12,257,320
Royalties	3,361,748	595,269	1,063,102
Restructuring	242,445	350,137	633,238
Total operating expenses	62,869,033	78,523,805	163,708,660
Operating loss	(34,240,678)	(63,563,756)	(157,668,118)
Interest and other income	1,354,337	4,901,106	5,496,081
Interest expense	(3,784,648)	(4,067,795)	(5,075,848)
Loss before provision for income taxes	(36,670,989)	(62,730,445)	(157,247,885)
Provision for income taxes		58,118	145,313
Net loss	\$ (36,670,989)	\$ (62,788,563)	\$ (157,393,198)
Weighted average shares:			
Basic and diluted	41,466,361	33,936,317	20,789,388
Net loss per share, basic and diluted	\$ (0.88)	\$ (1.85)	\$ (7.57)

See accompanying notes.

**Table of Contents****EPIX PHARMACEUTICALS, INC.****CONSOLIDATED STATEMENTS OF STOCKHOLDERS EQUITY (DEFICIT)**

	Common Stock		Additional	Accumulated	Accumulated	Total
	Shares	Amount	Paid-In	Deficit	Other	Stockholders
			Capital		Comprehensive	Equity
					Income/(loss)	(Deficit)
Balance at December 31, 2005	15,523,207	\$ 155,232	\$ 204,833,760	\$ (187,975,500)	\$ (66,198)	\$ 16,947,294
Issuance of common stock under employee stock purchase plan	11,165	112	59,863			59,975
Issuance of common stock upon exercise of options	360,018	3,600	454,124			457,724
Sale of common stock to GlaxoSmithKline	3,009,027	30,090	17,469,910			17,500,000
Stock-based compensation expense			4,203,663			4,203,663
Cash paid for fractional shares	(29)		(205)			(205)
Issuance of common stock in connection with merger	13,621,338	136,213	85,963,747			86,099,960
Net loss				(157,393,198)		(157,393,198)
Available-for-sale marketable securities unrealized gain					103,506	103,506
Comprehensive loss						(157,289,692)
Balance at December 31, 2006	32,524,726	325,247	312,984,862	(345,368,698)	37,308	(32,021,281)
Issuance of common stock under employee stock purchase plan	54,731	547	203,257			203,804
Issuance of common stock upon exercise of options	361,154	3,612	414,824			418,436
Sale of common stock	5,245,468	52,454	14,957,898			15,010,352
			4,775,152			4,775,152

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Stock-based compensation expense						
Issuance of common stock in connection with merger	3,167,000	31,670	12,953,031			12,984,701
Net loss				(62,788,563)		(62,788,563)
Available-for-sale marketable securities unrealized gain					125,752	125,752
Comprehensive loss						(62,662,811)
Balance at December 31, 2007	41,353,079	413,530	346,289,024	(408,157,261)	163,060	(61,291,647)
Issuance of common stock under employee stock purchase plan	52,815	528	73,126			73,654
Issuance of common stock upon exercise of options	186,215	1,862	182,526			184,388
Sale of common stock	94,627	947	39,129			40,076
Stock-based compensation expense	227,955	2,280	3,734,228			3,736,508
Net loss				(36,670,989)		(36,670,989)
Available-for-sale marketable securities unrealized loss					(163,060)	(163,060)
Comprehensive loss						(36,834,049)
Balance at December 31, 2008	41,914,691	\$ 419,147	\$ 350,318,033	\$ (444,828,250)	\$	\$ (94,091,070)

See accompanying notes.

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**Table of Contents****EPIX PHARMACEUTICALS, INC.****CONSOLIDATED STATEMENTS OF CASH FLOWS**

	<b>Year Ended December 31,</b>		
	<b>2008</b>	<b>2007</b>	<b>2006</b>
Operating activities:			
Net loss	\$ (36,670,989)	\$ (62,788,563)	\$ (157,393,198)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation, amortization and asset write offs	1,873,101	1,959,542	1,548,422
Write-off of acquired in-process research and development			123,500,000
Stock-based compensation expense	3,736,508	4,775,152	4,203,663
Noncash interest expense (credit) from embedded derivative		(771,592)	936,536
Merger consideration interest paid in common stock		975,432	
Amortization of deferred financing costs	528,678	510,184	492,337
Accretion of discount on available-for-sale securities	(758,704)	(2,582,393)	(593,665)
Changes in operating assets and liabilities, exclusive of amounts acquired from the merger with Predix:			
Accounts receivable	(1,112,698)	(593,029)	852,920
Prepaid expenses and other current assets	99,172	1,051,766	(282,827)
Other assets and liabilities	(402,436)	2,421,205	2,073,119
Accounts payable	(2,480,536)	1,557,067	216,567
Accrued expenses	1,546,970	403,991	(5,892,204)
Contract advances	(1,039,914)	114,122	(1,507,470)
Merger consideration payable		(465,517)	465,517
Deferred revenue	(1,768,377)	(3,705,947)	15,741,238
Net cash used in operating activities	(36,449,225)	(57,138,580)	(15,639,045)
Investing activities:			
Cash paid for merger with Predix, net of cash acquired		(5,257,707)	(7,142,601)
Purchases of marketable securities	(24,572,340)	(108,710,354)	(124,598,368)
Sales or redemptions of marketable securities	77,087,112	138,317,442	98,310,699
Purchases of fixed assets	(830,578)	(4,161,704)	(1,314,374)
Other investing activities	130,821	293,073	(243,327)
Net cash provided by (used in) investing activities	51,815,015	20,480,750	(34,987,971)
Financing activities:			
Principal payments of notes payable			(9,516,380)
Principal payments on capital leases	(225,198)	(149,257)	(44,536)
Proceeds from sale of common stock	40,076	15,010,352	17,500,000
Proceeds from stock option exercises	184,388	418,436	457,724
Proceeds from employee stock purchase plan	73,654	203,804	59,975
Cash paid for fractional shares from reverse stock split			(205)

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Net cash provided by financing activities	72,920	15,483,335	8,456,578
Net increase (decrease) in cash and cash equivalents	15,438,710	(21,174,495)	(42,170,438)
Cash and cash equivalents at beginning of year	9,157,973	30,332,468	72,502,906
Cash and cash equivalents at end of year	\$ 24,596,683	\$ 9,157,973	\$ 30,332,468
Supplemental cash flow information:			
Cash paid for interest	\$ 3,038,739	\$ 3,552,440	\$ 3,383,774
Cash paid for taxes	\$	\$ 58,118	\$ 145,313
Supplemental disclosure of noncash financing and investing activities:			
Milestone obligation paid in common stock	\$	\$ 12,009,268	\$
Purchases of fixed asset with capital lease	\$ 298,319	\$ 325,154	\$

See accompanying notes.

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**EPIX PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

**1. Business**

EPIX Pharmaceuticals, Inc. ( EPIX or the Company ) is a biopharmaceutical company focused on discovering and developing novel therapeutics through the use of its proprietary and highly efficient in silico drug discovery platform. The Company has a pipeline of internally-discovered drug candidates currently in clinical development to treat diseases of the central nervous system and lung conditions. The Company also has collaborations with SmithKline Beecham Corporation (GlaxoSmithKline), Amgen Inc. and Cystic Fibrosis Foundation Therapeutics, Incorporated (CFFT).

Since the Company's acquisition of Predix Pharmaceuticals Holdings, Inc. ( Predix ) in August 2006, its focus has been on the development of therapeutic drug products. The focus of the Company's 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. The Company believes its 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, the Company believes that it can rapidly identify and optimize highly selective drug candidates. The Company typically focuses 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 its clinical-stage therapeutic programs, the Company used its 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. The Company has moved each of these drug candidates into clinical trials in less than 18 months from lead identification. The Company believes its drug discovery technology and approach enables it to efficiently and cost-effectively discover and develop GPCR and ion channel-targeted drugs.

The Company's blood-pool magnetic resonance angiography imaging agent, Vasovist, was approved by the U.S. Food and Drug Administration ( FDA ) for marketing in the United States in December 2008, and has been approved for marketing in over 30 countries outside of the United States. Effective March 1, 2009, Bayer Schering Pharma AG, Germany ( Bayer Schering ) terminated the strategic collaboration agreement between the Company and Bayer Schering relating to Vasovist. Accordingly, the worldwide commercial rights for Vasovist were transferred back to the Company on such date. It is the Company's intention to sell the commercial rights to Vasovist. However, there is no guarantee that it will be able to do so. Upon a sale of the commercial rights to Vasovist, the Company will be required to reimburse Bayer Schering for a portion of their development costs. The reimbursement will be based on pre-defined percentages of the development costs, allocated to each territory for which the commercial rights are sold, with full worldwide rights amounting to a \$33 million reimbursement to Bayer Schering.

***Going Concern Uncertainty and Management's Plans***

The Company has experienced and continues to experience negative cash flows from operations and it expects to continue to incur net losses in the foreseeable future. Accordingly, in March 2009 and October 2008, the Company implemented workforce reductions that eliminated approximately 62% of its workforce in connection with efforts to reduce its cost structure. The Company also narrowed the focus of its research and development efforts to its lead clinical programs, PRX-03140 being developed for the treatment of Alzheimer's disease and PRX-08066 being developed for the treatment of pulmonary hypertension associated with chronic obstructive pulmonary disease (COPD), as well as its partnered preclinical programs with GlaxoSmithKline and CFFT. In connection with the March

2009 workforce reduction, the Company entered into a letter agreement with GlaxoSmithKline allowing the Company to reduce its research and development obligations under the collaboration agreement, during the period from March 13, 2009 to September 13, 2009, for programs other than the PRX-03140 program.

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**EPIX PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

The accompanying financial statements have been prepared in conformity with accounting principles generally accepted in the United States, which contemplate continuation of the Company as a going concern. As of December 31, 2008, the Company had \$24.6 million of cash and cash equivalents to fund its operations. The Company estimates that its cash and cash equivalents, along with anticipated revenue that the Company expects to earn during the first half of 2009, will fund its operations only through August 2009. This projection is based on the Company's current cost structure and the Company's current expectations regarding operating expenses and anticipated revenues. In addition, on February 4, 2009, the Company received notice from the Listing Qualifications Panel of the NASDAQ Stock Market LLC (NASDAQ) that NASDAQ has determined to continue the listing of the Company's common stock on the NASDAQ Global Market subject to its compliance with Marketplace Rule 4450(b)(1)(A), which requires the Company to maintain a market value of its common stock of at least \$50,000,000 for at least 10 consecutive days on or prior to May 11, 2009. As of March 10, 2009, the Company was not in compliance with the requirement for continued inclusion on NASDAQ. If it does not regain compliance with the rules for continued listing on NASDAQ, the Company's common stock will be delisted from NASDAQ. If the Company's common stock is delisted from NASDAQ, the holders of its \$100 million aggregate principal amount of 3% Convertible Senior Notes could redeem their notes at face value, plus accrued and unpaid interest. The Company currently does not have sufficient funds to repurchase more than a nominal amount of the notes if tendered by the holders. Accordingly, it will need to raise significant additional capital to fund its operations beyond August 2009 or if the Company is required to redeem the notes. The Company plans to generate funds through a potential sale of the commercial rights to Vasovist and by pursuing additional financing strategies. If the Company is unable to obtain such additional funds, it will not be able to sustain its operations and would be required to cease its operations and/or seek bankruptcy protection. Given the difficult current economic environment, the Company believes that it will be difficult to raise additional funds and there can be no assurance as to the availability of additional financing or the terms upon which additional financing may be available. As a result of these conditions, there is substantial doubt regarding the Company's ability to continue as a going concern. The accompanying financial statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from the possible inability of the Company to continue as a going concern.

**2. Significant Accounting Policies**

*Principles of Consolidation*

The consolidated financial statements include the financial statements of the Company and those of its wholly owned subsidiary in Israel. All material intercompany balances and transactions have been eliminated.

*Use of Estimates*

The preparation of financial statements in conformity with accounting principles generally accepted in the U.S. requires the Company to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

*Translation of Foreign Currencies*



The functional currency of the Company's foreign subsidiary is the U.S. dollar. The subsidiary's financial statements are remeasured into U.S. dollars using current rates of exchange for monetary assets and liabilities and historical rates of exchange for nonmonetary assets.

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**EPIX PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

***Cash Equivalents***

The Company considers investments with an original maturity of three months or less when purchased to be cash equivalents. Cash equivalents consist of money market accounts, government-sponsored agency securities and commercial paper.

***Marketable Securities***

The Company accounts for marketable securities in accordance with Statement of Financial Accounting Standards ( SFAS ) No. 115, *Accounting for Certain Investments in Debt and Equity Securities* ( SFAS 115 ). SFAS 115 establishes the accounting and reporting requirements for all debt securities and for investments in equity securities that have readily determinable fair values. Marketable securities consist of investment-grade corporate bonds, asset-backed debt securities and government-sponsored agency debt securities. The Company classifies its marketable securities as available-for-sale and, as such, carries the investments at fair value, with unrealized holding gains and losses included in accumulated other comprehensive income or loss. The cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion are included in interest income. Realized gains or losses and declines in value judged to be other-than-temporary on available-for-sale securities are included in interest and other income. The cost of securities is based on the specific identification method.

***Fair Value of Financial Instruments***

The Company adopted SFAS No. 157 *Fair Value Measurements* ( SFAS 157 ) on January 1, 2008, which did not have a material impact on the Company's financial condition or results of operations. SFAS 157 defines fair value, establishes a framework for measuring fair value and expands disclosures about fair value measurements. The standard creates a fair value hierarchy which prioritizes the inputs to valuation techniques used to measure fair value into three broad levels as follows: Level 1 inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities; Level 2 inputs are inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly; and Level 3 inputs are unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability. Financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. At December 31, 2008 the Company did not have any assets or liabilities measured at fair value.

On January 1, 2008, the Company adopted SFAS No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities Including an Amendment of FASB Statement No. 115* ( SFAS 159 ). SFAS 159 permits an entity to choose to measure many financial instruments and certain other items at fair value at specified election dates. Subsequent unrealized gains and losses on items for which the fair value option has been elected will be reported in earnings. The Company did not elect to measure any additional financial instruments or other items at fair value and the adoption of SFAS 159 did not have a material impact on the Company's financial condition or results of operations.

The Company's financial instruments, consisted of cash and cash equivalents, marketable securities, accounts receivable, accounts payable and debt, all of which are recorded at historical cost except for marketable securities. The carrying value of cash equivalents, accounts receivable and accounts payable approximates fair value due to their short term nature. The carrying value of the available-for-sale marketable securities is further discussed in Note 3. The

fair value of the 3.0% convertible senior notes, which is based on trading activity of the notes, was approximately \$35.0 million and \$68.0 million at December 31, 2008 and 2007, respectively.

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**EPIX PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

***Concentrations of Credit Risk***

Financial instruments that potentially subject the Company to concentrations of credit risk primarily consist of cash equivalents and accounts receivable. In accordance with the Company's investment policy, investments are principally restricted to U.S. government securities, high-grade bank obligations, high-grade corporate bonds, commercial paper, asset-backed securities and certain money market funds. Although the vast majority of the Company's \$24.6 million of cash and cash equivalents were invested through one investment advisor as of December 31, 2008, the credit risk exposure of its investments was limited because of a diversified portfolio that included money market funds, government-sponsored agency securities and commercial paper. The Company has not experienced any credit losses in these accounts and does not believe it is exposed to any significant credit risk on these funds.

To date, the Company's revenues have been generated from a limited number of customers. For the years ended December 31, 2008, 2007 and 2006, GlaxoSmithKline accounted for 76%, 53% and 1%, respectively, of total revenues and CFFT accounted for 17%, 25% and 15%, respectively, of total revenues.

Receivables from GlaxoSmithKline and CFFT represented 84% and 16%, respectively, of the Company's accounts receivable balance at December 31, 2008. Receivables from GlaxoSmithKline and CFFT represented 49% and 51%, respectively, of the Company's accounts receivable balance at December 31, 2007. The Company believes the credit risk associated with these collaborators is not significant.

***Property and Equipment***

Property and equipment are recorded at historical cost. Depreciation on laboratory equipment, furniture and fixtures and other equipment is determined using the straight-line method over the estimated useful lives of the related assets, ranging from 2 to 5 years. Leasehold improvements are amortized using the straight-line method over the shorter of the asset life or the remaining life of the lease. Expenditures for maintenance and repairs are charged to expense as incurred; improvements which extend the life or use of equipment are capitalized.

***Long-Lived Assets***

In accordance with SFAS No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets*, the Company recognizes impairment losses on long-lived assets when indicators of impairment are present and future undiscounted cash flows are insufficient to support the assets' recovery.

***Other Assets***

Included in other assets at December 31, 2008 is restricted cash in the amount of \$1.2 million. Restricted cash consists of amounts held in deposit at a financial institution to collateralize standby letters of credit in the name of the Company's landlords in accordance with certain facility lease agreements.

***Goodwill***

The Company assesses the realizability of goodwill annually and whenever events or changes in circumstances indicate it may be impaired. The Company completed its annual test for impairment on July 1, 2008 and, based on

impairment indicators that were primarily the result of significant uncertainty about the Company's ability to raise capital given market conditions, tested for impairment as of December 31, 2008. When testing for goodwill impairment, the Company performs a step I goodwill impairment test to identify a potential impairment in accordance with SFAS No. 142, *Goodwill and Other Intangible Assets*. In doing so, the Company compares the fair value of the Company, the sole reporting unit, with its carrying amount. If the carrying amount exceeds the fair value, goodwill may be impaired and a step II goodwill impairment test would be performed to measure the amount of any impairment loss. As the Company had fair value in excess

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**EPIX PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

of the stockholders' deficit balance as of the testing dates, the Company passed the step I impairment test, and accordingly goodwill was not impaired as of December 31, 2008.

***Income Taxes***

The Company provides for income taxes under SFAS No. 109, *Accounting for Income Taxes*. Under this method, deferred taxes are recognized using the liability method, whereby tax rates are applied to cumulative temporary differences between carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes and are based on when and how they are expected to affect the tax return. A valuation allowance is provided to the extent that there is uncertainty as to the Company's ability to generate sufficient taxable income in the future to realize the benefit from its net deferred tax asset.

***Segment Information***

SFAS No. 131, *Disclosure about Segments of an Enterprise and Related Information*, establishes standards for reporting information regarding operating segments and for related disclosures about products and services and geographical areas. The Company operates in one business segment, which is the development of pharmaceutical products. Substantially all of the Company's assets are located within the United States and substantially all of the Company's revenues are generated within the United States.

***Revenue***

The Company recognizes revenue relating to collaborations in accordance with the SEC's Staff Accounting Bulletin (SAB) No. 104, *Revenue Recognition in Financial Statements*, (SAB 104). Revenue under collaborations may include the receipt of non-refundable license fees, milestone payments, reimbursement of research and development costs and royalties.

The Company recognizes nonrefundable upfront license fees and guaranteed, time-based payments that require continuing involvement in the form of research and development as revenue ratably over the development period. When the period of deferral cannot be specifically identified from the contract, the Company estimates the period based upon other critical factors contained within the contract. The Company continually reviews such estimates which could result in a change in the deferral period and might impact the timing and amount of revenue recognized.

Milestone payments which represent a significant performance risk are recognized as product development revenue when the performance obligations, as defined in the contract, are achieved. Performance obligations typically consist of significant milestones in the development life cycle of the product candidate, such as the filing of investigational new drug applications, initiation of clinical trials, filing for approval with regulatory agencies and approvals by regulatory agencies. Milestone payments that do not represent a significant performance risk are recognized ratably over the development period.

Reimbursements of research and development costs are recognized as product development revenue as the related costs are incurred.

Royalties are recognized as revenue when earned, are reasonably estimable and collection is probable, which is typically upon receipt of royalty reports from the licensee or cash.

*Product development revenue*

The Company is a party to collaboration agreements with GlaxoSmithKline and CFFT. Under the agreements, the Company receives cost reimbursements and research funding and may earn milestone payments in accordance with the terms of the agreements. The Company recognizes as revenue the

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**EPIX PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

reimbursements of research and development costs as the related costs are incurred. As the Company is the party responsible for providing the research services, the Company recognizes the reimbursement of the costs associated with the Company's research efforts as revenue, not as a net research expense. The Company recognizes milestone payments as revenue when the related performance obligation, as defined in the agreement, has been achieved.

In June 2000, the Company entered into a strategic collaboration agreement with Bayer Schering, whereby each party to the agreement shared equally in Vasovist development costs and the Company received royalties related to non-U.S. sales. The Company recognizes as revenue costs incurred by the Company in excess of the Company's obligation under the agreement to expend 50% of the costs to develop Vasovist. This revenue is recognized in the same period in which the costs are incurred. With respect to payments due to Bayer Schering, if any, in connection with the Vasovist development program, the Company recognizes such amounts as a reduction in revenue at the time Bayer Schering performs the research and development activities for which the Company is obligated to pay Bayer Schering. The additional payments made by Bayer Schering to the Company represent revenue to the Company because the Company is providing additional services to Bayer Schering which Bayer Schering was contractually obligated to perform itself. In September 2008 Bayer Schering terminated the collaboration agreement effective March 1, 2009. Accordingly, the worldwide commercial rights for Vasovist transferred back to the Company on such date. If the Company were to sell the commercial rights to Vasovist, the Company would be required to reimburse Bayer Schering for a portion of their development costs. The reimbursement will be based on pre-defined percentages of the development costs, allocated to each territory for which the commercial rights are sold, with full worldwide rights amounting to a \$33 million reimbursement to Bayer Schering.

In May 2003, the Company entered into a development agreement with Bayer Schering for EP-2104R and a collaboration agreement with Bayer Schering for MRI research. Under the EP-2104R development agreement, Bayer Schering agreed to make fixed payments totaling approximately \$9.0 million to the Company over a two year period, which began in the second quarter of 2003 and ended in the fourth quarter of 2004, to cover a portion of the Company's expenditures for the EP-2104R feasibility program. The Company recognized revenue from Bayer Schering for the feasibility program in proportion to actual cost incurred relative to the estimated total program costs. During the third quarter of 2006, the Company completed its work on the feasibility program. On July 13, 2006, Bayer Schering determined not to exercise its option for the development of EP-2104R. Under the terms of the agreement, EPIX retained full rights to the EP-2104R program. Revenue under the MRI research collaboration was recognized at the time services were provided. The MRI research program was completed in the second quarter of 2006.

Payments received by the Company from collaboration partners in advance of the Company performing research and development activities are recorded as liabilities in the balance sheets.

*Royalty revenue*

The Company receives a royalty on Bayer Schering's sales of Vasovist outside of the United States and on sales of Primovist. Commercial launch of Vasovist in the European Union began on a country-by-country basis in the second quarter of 2006. Effective on March 1, 2009, the termination date of the Company's collaboration agreement with Bayer Schering for Vasovist, Bayer Schering is no longer authorized to sell Vasovist and as such the Company will no longer receive royalties from Bayer Schering from their sales of Vasovist. The Company recognizes royalty revenue from sales of Vasovist and Primovist in the quarter when Bayer Schering reports those sales to the Company.



The Company also earned royalty revenue pursuant to its sub-license on certain of its patents to Bracco Imaging S.p.A. ( Bracco ). Due to the expiration of patents, the royalty revenue from Bracco ended in the second quarter of 2007.

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**EPIX PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

*License fee revenue*

The Company recognizes revenue from non-refundable license fees and milestone payments, not specifically tied to a separate earnings process, ratably over the period during which the Company has a substantial continuing obligation to perform services under the contract. When milestone payments are specifically tied to a separate earnings process, revenue is recognized when the specific performance obligations associated with the payment are completed.

In December 2006, the Company established a worldwide multi-target strategic collaboration with GlaxoSmithKline to discover, develop and market novel medicines targeting four G-protein coupled receptors (GPCRs) for the treatment of a variety of diseases, including EPIX's novel 5-HT<sub>4</sub> partial agonist program, PRX-03140, in early-stage clinical development for the treatment of Alzheimer's disease. EPIX received \$17.5 million of up front payments which were recorded as deferred revenue and will be recorded as revenue ratably from the time of payment until the expiration of the contract in December 2020.

In connection with the acquisition of Predix, the Company is recognizing license fee revenue for arrangements that Predix had with both Amgen and CFFT. The Company ascribed \$3.4 million and \$0.2 million of value to these arrangements, respectively, on the date of acquisition based upon the fair value of the remaining services to be provided by EPIX. The deferred revenue is being recognized ratably over the period in which the Company is required to provide services, which was October 2007 for Amgen and July 2009 for CFFT. In April 2008, the Company entered into a new research agreement with CFFT which extended the period of development services for up to 12 additional years through April 2020.

In September 2001, the Company sub-licensed certain patents to Bracco and received a \$2.0 million license fee from Bracco. This license fee was included in deferred revenue and was recorded as revenue ratably from the time of the payment until the expiration of MGH's patents, which occurred in the European Union in May 2006 and in the United States in November 2006.

As part of the Company's strategic collaboration agreement with Bayer Schering for Vasovist, the Company granted Bayer Schering an exclusive license to co-develop and market Vasovist worldwide, exclusive of Japan. Later in 2000, the Company amended this strategic collaboration agreement to grant Bayer Schering exclusive rights to develop and market Vasovist in Japan. The Company received a \$3.0 million license fee from Bayer Schering in connection with that amendment. This license fee is included in deferred revenue. The Company is amortizing this revenue over the term of the contract through March 1, 2009.

Pursuant to an earlier collaboration agreement with Covidien Ltd., the Company recorded \$4.4 million of deferred revenue. The Company amortized this revenue over the term of the contract and fully recognized the revenue upon the approval of Vasovist in December 2008.

***Research and Development Expenses***

Research and development expenses, including those associated with technology and licenses, are expensed as incurred. Research and development costs primarily include employee salaries and related costs, third-party service costs, the cost of preclinical and clinical trials, supplies, consulting expenses, facility costs and certain overhead costs.

In order to conduct research and development activities and compile regulatory submissions, the Company enters into contracts with vendors who render services over extended periods of time. Typically, the Company enters into three types of vendor contracts: time-based, patient-based or a combination thereof. Under a time-based contract, using critical factors contained within the contract, usually the stated duration of the contract and the timing of services provided, the Company records the contractual expense for each service provided under the contract ratably over the period during which the Company estimates the service will be performed. Under a patient-based contract, the Company first determines an appropriate per patient cost using critical

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Table of Contents**EPIX PHARMACEUTICALS, INC.****NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

factors contained within the contract, which include the estimated number of patients and the total dollar value of the contract. The Company then records expense based upon the total number of patients enrolled in the clinical study ratably during the treatment period. On a quarterly basis, the Company reviews the assumptions for each contract in order to reflect the Company's most current estimate of the costs incurred under each contract. Adjustments are recorded in the period in which the revisions are estimable.

***Loss Per Share***

The Company computes loss per share in accordance with the provisions of SFAS No. 128, *Earnings per Share*. Basic net loss per share is based upon the weighted-average number of common shares outstanding and excludes the effect of dilutive common stock issuable from stock options, warrants, restricted stock units, convertible debt and merger consideration. In computing diluted loss per share, only potential common shares that are dilutive, or those that reduce earnings per share, are included. The issuance of common stock from stock options, warrants, restricted stock units, convertible debt and merger consideration is not assumed if the result is anti-dilutive, such as when a loss is reported.

Common stock potentially issuable but excluded from the calculation of dilutive net loss per share for the years ended December 31, 2008, 2007 and 2006 because their inclusion would have been antidilutive consisted of the following:

	<b>2008</b>	<b>2007</b>	<b>2006</b>
Stock options, awards and warrants	3,772,436	3,847,386	3,427,107
Shares issuable on conversion of 3% Convertible Senior Notes(A)	2,239,393	2,239,393	2,239,393
Shares issuable in satisfaction of merger consideration payable(B)			3,008,726
Total	6,011,829	6,086,779	8,675,226

(A) Each \$1,000 of senior notes is convertible into 22.39 shares of the Company's common stock representing a conversion price of approximately \$44.66 per share if (1) the price of the Company's common stock trades above 120% of the conversion price for a specified time period, (2) the trading price of the senior notes is below a certain threshold, (3) the senior notes have been called for redemption, or (4) specified corporate transactions have occurred. None of these conversion triggers have occurred as of December 31, 2008.

(B) Share amount calculated as if the merger consideration was payable as of December 31, 2006. Actual settlement occurred on October 29, 2007 as the Company issued 3,167,000 shares of common stock and paid \$5.8 million in cash.

***Comprehensive Loss***

In accordance with SFAS No. 130, *Reporting Comprehensive Income* components of comprehensive loss include net loss and certain transactions that have generally been reported in the statements of stockholders' equity (deficit). Other comprehensive loss is comprised of unrealized gains or losses on available-for-sale marketable securities.

***Employee Stock Compensation***

The Company applies the provisions of SFAS No. 123(R), *Share-Based Payment - An Amendment of FASB Statements No. 123 and 95* ( SFAS 123(R) ), to share-based payments. SFAS 123 (R) requires companies to recognize share-based payments to employees as compensation expense using the fair value method. The fair value of stock options and shares purchased pursuant to the Company's employee stock

**Table of Contents****EPIX PHARMACEUTICALS, INC.****NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

purchase plan is calculated using the Black-Scholes valuation model. The fair value of restricted stock units is based on the intrinsic value on the date of grant. Under the fair value recognition provisions of SFAS 123(R), stock-based compensation expense, measured at the grant date based on the fair value of the award, is recognized ratably over the service period. The expense recognized over the service period includes an estimate of awards that will be forfeited.

***Reclassifications***

Certain items in the prior year's consolidated financial statements have been reclassified to conform to the current presentation of the financial statements.

***Recent Accounting Pronouncements***

In December 2007, the FASB issued SFAS No. 141(R), *Business Combinations* (SFAS 141(R)), which provides greater consistency in the accounting and financial reporting of business combinations. It requires the acquiring entity in a business combination to recognize all assets acquired and liabilities assumed in the transaction, establishes the acquisition-date fair value as the measurement objective for all assets acquired and liabilities assumed, and requires the acquirer to disclose the nature and financial effect of the business combination. SFAS 141(R) is effective for fiscal years beginning after December 15, 2008. The adoption of SFAS 141(R) is not anticipated to have a significant impact on the Company's financial position and results of operations.

In May 2008, the FASB issued FSP APB 14-1, *Accounting for Convertible Debt Instruments That May Be Settled in Cash upon Conversion (Including Partial Cash Settlement)* (FSP APB 14-1), which clarifies that convertible debt instruments that may be settled in cash upon conversion (including partial cash settlement) are not addressed by paragraph 12 of APB Opinion No. 14, *Accounting for Convertible Debt and Debt Issued with Stock Purchase Warrants*. In addition, FSP APB 14-1 indicates that issuers of such instruments generally should separately account for the liability and equity components in a manner that will reflect the entity's nonconvertible debt borrowing rate when interest cost is recognized in subsequent periods. FSP APB 14-1 is effective for the Company beginning January 1, 2009 with early adoption prohibited. The adoption of FSP APB 14-1 will not impact on the Company's financial position and results of operations as the provisions of FSP APB 14-1 do not apply to the Company's convertible debt.

**3. Marketable Securities**

The Company had no marketable securities at December 31, 2008. The estimated fair value of marketable securities at December 31, 2007 was determined based on broker quotes or quoted market prices or rates for the same or similar instruments. The estimated fair value and cost of marketable securities are as follows at December 31:

	<b>2007</b>	
	<b>Fair Value</b>	<b>Cost</b>
Corporate bonds	\$ 2,565,474	\$ 2,566,837
Commercial paper	35,357,829	35,206,400
Asset backed securities	13,524,757	13,511,763

Certificates of deposit	471,068	471,068
	\$ 51,919,128	\$ 51,756,068

All of the Company's marketable securities as of December 31, 2007 are classified as available-for-sale and by contractual maturity are due within one year.

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Table of Contents**EPIX PHARMACEUTICALS, INC.****NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

Gross unrealized gains and losses on marketable securities amounted to \$164,423 and \$1,363 at December 31, 2007, respectively. The aggregate fair value of investments with unrealized losses was \$2.5 million at December 31, 2007. There were no realized gains or losses on marketable securities in 2008, 2007 and 2006.

**4. Property and Equipment**

Property and equipment consist of the following:

	<b>December 31,</b>	
	<b>2008</b>	<b>2007</b>
Leasehold improvements	\$ 3,804,245	\$ 3,766,584
Laboratory equipment	3,194,205	2,777,731
Furniture, fixtures and other equipment	3,445,405	3,020,935
	10,443,855	9,565,250
Less accumulated depreciation and amortization	(5,143,173)	(3,520,364)
	\$ 5,300,682	\$ 6,044,886

Depreciation expense for years ended December 31, 2008, 2007 and 2006 was \$1.9 million, \$1.9 million and \$1.3 million, respectively.

**5. Accrued Expenses**

Accrued expenses consist of the following:

	<b>December 31,</b>	
	<b>2008</b>	<b>2007</b>
Accrued contractual product development expenses	\$ 2,501,087	\$ 3,407,600
Accrued compensation	2,359,359	2,184,368
Royalties	2,513,711	9,861
Other accrued expenses	2,272,352	2,497,710
	\$ 9,646,509	\$ 8,099,539

**6. Restructuring Charges**



The Company has experienced and continues to experience negative cash flows from operations. Accordingly, in October 2008, the Company eliminated approximately 23% of its workforce in connection with efforts to reduce its cost structure. The Company also narrowed the focus of its research and development efforts to its lead clinical programs, PRX-03140 being developed for the treatment of Alzheimer's disease and PRX-08066 being developed for the treatment of pulmonary hypertension associated with chronic obstructive pulmonary disease, as well as its partnered preclinical programs with GlaxoSmithKline and CFFT. In connection with this workforce reduction, the Company incurred a restructuring charge of approximately \$0.2 million for cash payments of one-time employee termination benefits, including severance, and other benefits. The restructuring was completed in the fourth quarter of 2008.

During the second quarter of 2007, the Company incurred a restructuring charge of \$0.5 million for the consolidation of its leased laboratory facility in Cambridge, Massachusetts into the Company's Lexington, Massachusetts facility. The charge consisted primarily of future lease costs through the end of 2007. The consolidation was completed during the second quarter of 2007. In addition, during the second quarter of 2007, the Company recorded a reduction of its 2006 restructuring charge in the amount of \$0.1 million

**Table of Contents****EPIX PHARMACEUTICALS, INC.****NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

relating to a reduction in the amount of square footage leased at the Company's former headquarters location in Cambridge, Massachusetts.

The 2006 restructuring costs included approximately \$0.4 million related to a restructuring plan implemented in the fourth quarter of 2005 for additional severance costs as well as costs related to vacating certain leased space and the write-off of leasehold improvements. In addition, in the third quarter of 2006, the Company recorded additional restructuring charges of \$0.2 million for facility exit costs related to the consolidation of the Company's Cambridge, MA headquarters into the former Predix headquarters in Lexington, MA. These costs primarily consisted of future lease payments through the end of 2007 and the write off of leasehold improvements.

The following table displays the restructuring activity and liability balances:

	<b>Severance</b>	<b>Asset Write Off</b>	<b>Lease Obligation</b>	<b>Total</b>
Balance at December 31, 2005	\$ 971,828	\$	\$	\$ 971,828
2006 restructuring charge	134,642	177,906	320,690	633,238
Cash payments	(1,106,470)		(90,714)	(1,197,184)
Non-cash payments		(177,906)		(177,906)
Balance at December 31, 2006			229,976	229,976
2007 restructuring charge			482,535	482,535
Cash payments			(580,113)	(580,113)
Reduction of 2006 restructuring charge			(132,398)	(132,398)
Balance at December 31, 2007				
2008 restructuring charge	242,445			242,445
Cash payments	(242,445)			(242,445)
Balance at December 31, 2008	\$	\$	\$	\$

**7. Financing Arrangements*****Convertible Debt***

In June 2004, the Company completed a sale, pursuant to Rule 144A under the Securities Act of 1933, of \$100.0 million of 3% convertible senior notes due 2024 for net proceeds of approximately \$96.4 million. The Company has the right to redeem the notes on or after June 15, 2009 at an initial redemption price of 100.85%, plus accrued and unpaid interest. Noteholders may require the Company to repurchase the notes at par, plus accrued and unpaid interest, on June 15, 2011, 2014 and 2019 and upon certain other events, including a change of control and termination of trading of the Company's common stock on the NASDAQ Stock Market. As of March 10, 2009, the Company is not in compliance with the rules for continued listing on the NASDAQ Stock Market. The Company has

until May 11, 2009 to meet the listing requirements; otherwise the Company's common stock will be delisted from the NASDAQ Stock Market.

Each \$1,000 of senior notes is convertible into 22.39 shares of the Company's common stock representing a conversion price of approximately \$44.66 per share if (1) the price of the Company's common stock trades above 120% of the conversion price for a specified time period, (2) the trading price of the senior notes is below a certain threshold, (3) the senior notes have been called for redemption, or (4) specified corporate transactions have occurred. None of these conversion triggers has occurred as of December 31, 2008. Each of the senior notes is also convertible into the Company's common stock in certain other circumstances. The senior notes bear an interest rate of 3%, payable semiannually on June 15 and December 15. Interest payments

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Table of Contents**EPIX PHARMACEUTICALS, INC.****NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

of \$3.0 million were made during each of the years ended December 31, 2008, 2007, and 2006. The senior notes are unsecured.

In connection with the issuance of the senior notes, the Company incurred \$3.65 million of issuance costs, which primarily consisted of investment banker fees and legal and other professional fees. The costs are being amortized as interest expense using the effective interest method over the term from issuance through the first date that the holders are entitled to require repurchase of the senior notes (June 2011). For the years ended December 31, 2008, 2007 and 2006, amortization of the issuance costs was \$528,678, \$510,184, and \$492,337, respectively.

**8. Commitments and Contingencies***Leases*

The Company leases facilities in Lexington, MA, Princeton, NJ and facilities and vehicles in Ramat Gan, Israel under agreements that are accounted for as operating leases. On August 31, 2006, the Company entered into an amended lease agreement for its Lexington facility, which expanded the space under lease from approximately 29,000 square feet to approximately 57,000 square feet. The Company's facility leases generally provide for a base rent plus real estate taxes and certain operating expenses related to the leases. Certain of the Company's leases contain renewal options, escalating payments over the life of the lease and landlord allowances. Scheduled rent increases and landlord allowances are being amortized over the terms of the agreements using the straight-line method, and are included in other liabilities in the accompanying consolidated balance sheet. The Company leases certain equipment under capital lease agreements. The Company has assets under capital lease obligations amounting to \$0.8 million as of December 31, 2008. Amortization of such equipment is included in depreciation expense.

At December 31, 2008, future minimum commitments under all noncancellable capital and operating leases with initial or remaining terms of more than one year are as follows:

	<b>Capital Leases</b>	<b>Operating Leases</b>
2009	\$ 250,113	\$ 2,686,070
2010	169,797	2,515,166
2011	55,472	2,132,794
2012		1,725,868
2013		1,922,757
Thereafter		1,869,760
Total minimum lease payments	475,382	12,852,415
Less aggregate future sublease income		(1,403,030)
	475,382	\$ 11,449,385
Less amount representing interest	(39,654)	

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Present value of minimum lease payment	435,728
Less current portion of capital lease obligations	(221,585)
Capital lease obligations, net of current portion	\$ 214,143

The Company has subleased its leased facility in Princeton, NJ. Total rental expense amounted to \$1.9 million, \$3.1 million, and \$1.5 million for the years ended December 31, 2008, 2007 and 2006, respectively.

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**Table of Contents****EPIX PHARMACEUTICALS, INC.****NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)*****Other Commitments***

In November 2003, the Company entered into an intellectual property agreement with Martin R. Prince M.D., Ph.D. (the Prince Agreement). Under the terms of the Prince Agreement, Dr. Prince granted the Company certain discharges, licenses and releases in connection with the historic and future use of Vasovist by the Company and agreed not to sue the Company for intellectual property infringement related to the use of Vasovist. In consideration for Dr. Prince entering into this agreement, the Company paid him an upfront fee of \$850,000, issued him 88,000 shares of common stock valued at \$2.3 million (at the date of the agreement), agreed to pay him future royalties on sales of Vasovist and agreed to provide him with \$140,000 worth of Vasovist annually for the life of the agreement. The Company recorded a \$3.2 million charge to research and development expense in the fourth quarter of 2003 for the value of the cash and common stock consideration paid to Dr. Prince. During 2006, the obligation to provide Dr. Prince with \$140,000 of Vasovist annually was triggered and the Company recorded a \$0.9 million charge to research and development expense representing the present value of this obligation. Under the terms of the Prince Agreement, Dr. Prince may decide to defer delivery of all or a portion of the amount of Vasovist due to him in any given year to future years. The Prince Agreement expires based upon the last to expire patent or patent application as listed in the agreement, which is currently estimated to be in 2026. As of December 31, 2008 no Vasovist product had been provided to Dr. Prince.

**9. Stockholders Equity*****Common Stock***

On August 4, 2008, the Company entered into a Committed Equity Financing Facility (CEFF) with Kingsbridge Capital Limited (Kingsbridge) pursuant to which Kingsbridge committed to purchase, subject to certain conditions, up to the lesser of approximately 8.3 million shares of the Company's common stock or an aggregate of \$50.0 million of common stock during the three years following the execution of the CEFF. Based on the Company's stock price of \$0.48 on March 10, 2009, the Company is not able to sell shares under the CEFF and will continue to be restricted from any drawdown unless the Company's common stock price is at least \$1.25. In September 2008, the Company drew down on the CEFF and issued to Kingsbridge 94,627 shares of the Company's common stock, \$0.01 par value per share, at an aggregate purchase price of \$113,750. Under the CEFF, the Company is able to draw down funds in tranches of up to a maximum equivalent of 1.5 percent of the closing market value of its common stock on the last trading day prior to the commencement of the drawdown, or \$10.0 million, whichever is less, subject to certain conditions. The purchase price of these shares will be discounted between 6 to 12 percent from the volume-weighted average price of the Company's common stock for each of the eight trading days following the election to sell shares depending on the trading price at the time of the drawdown. Kingsbridge is not obligated to purchase shares at prices below \$1.25 per share or if the volume-weighted average price of the Company's common stock is below 90% of the closing market value of the Company's common stock on the trading day immediately preceding the commencement of the drawdown. The Company did not make any further drawdowns subsequent to September 30, 2008. In connection with the CEFF, the Company issued a warrant to Kingsbridge to purchase 400,000 shares of the Company's common stock at a price of \$2.4925 per share exercisable beginning on February 5, 2009 for a period of five years thereafter.

On November 9, 2007, the Company entered into Securities Purchase Agreements pursuant to which it sold in a private placement to institutional and accredited investors an aggregate of 5,245,468 shares of the Company's common stock, \$0.01 par value per share, at a per share purchase price of \$3.10, which represented a discount of approximately

15% to the closing bid price of the Common Stock as reported on the NASDAQ Global Market on November 8, 2007. Aggregate proceeds from the private placement, after deducting offering expenses, were approximately \$15.0 million. The closing of the private placement occurred on November 15, 2007. These shares were registered on Form S-1 in December 2007.

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**EPIX PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

In December 2006, the Company filed a shelf registration statement on Form S-3 with the Securities and Exchange Commission to allow the Company to issue, in one or more offerings, up to \$75 million in common stock, preferred stock or warrants. Pursuant to Instruction I.B.6 of Form S-3, the Company may offer securities registered on the shelf registration statement even though the market value of its equity securities held by non-affiliates, or public float, is less than \$75 million. However, for so long as its public float is less than \$75 million, in any 12-month period the Company is limited to selling such securities for an aggregate value of one-third of the Company's public float at such time.

In conjunction with the Company's collaboration agreement with GlaxoSmithKline entered into on December 11, 2006, the Company entered into a stock purchase agreement with GlaxoSmithKline. Pursuant to this agreement, GlaxoSmithKline purchased 3,009,027 shares of the Company's common stock for \$17,500,000.

***Equity Plans***

The Company maintains the following four equity compensation plans under which the Company's equity securities are authorized for issuance to our employees, directors and consultants: 2008 Stock Option and Incentive Plan (2008 Plan), Amended and Restated 1992 Incentive Plan (1992 Plan); Amended and Restated 1996 Director Stock Option Plan (1996 Director Plan); and Amended and Restated 2003 Stock Incentive Plan (2003 Plan). Upon approval of the 2008 Plan by stockholders on May 19, 2008, future grants under all other plans have been discontinued.

The 2008 Plan provides equity awards to be granted to employees, directors and consultants. A maximum of 6,000,000 shares may be issued under the 2008 Plan plus the number of shares underlying any awards that are forfeited, cancelled, repurchased or terminated under the 1992 Plan. The 2008 Plan provides for a share reduction formula in the pool of available shares, whereby the issuance of any full value award (i.e., an award other than a stock option or stock appreciation right) will reduce the pool of available shares by 1.5 shares. Stock options may be granted under the 2008 Plan either as options intended to qualify as incentive stock options (ISOs) under the Internal Revenue Code or as non-qualified stock options (NQSOs). Each option granted under the 2008 Plan has an exercise price equal to the fair market value of the underlying common stock on the date of grant. Stock options have a contractual term of ten years and generally vest over a period of four years. As of December 31, 2008, 5,876,390 shares are available for grant under the 2008 Plan.

The 1992 Plan provided equity awards to be granted to employees and consultants. The 1992 Plan provided for the grant of ISOs and NQSOs, stock appreciation rights, performance shares, and restricted stock or stock units. Awards under the 1992 Plan were granted to officers, employees and other individuals as determined by the compensation committee. The compensation committee also selected the participants and established the terms and conditions of each option or other equity right granted under the 1992 Plan, including the exercise price, the number of shares subject to options or other equity rights and the time at which such options become exercisable. The stock options have a contractual term of ten years and generally vest over a period of four or five years. As of December 31, 2008, shares of common stock are no longer available for grant under the 1992 Plan.

The 1996 Director Plan provided for stock option grants to the non-employee directors of the Company. Stock option awards were based upon the provisions included within the 1996 Director Plan or as determined by the compensation committee. The term of each option granted under the 1996 Director Plan is ten years from the date of grant. The exercise price for the options is equal to the fair value of the underlying shares at the date of grant. As of



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December 31, 2008, shares of common stock are no longer available for grant under the 1996 Director Plan.

In conjunction with the merger with Predix Pharmaceuticals Holdings, Inc in 2006, the Company assumed the 2003 Plan. The 2003 Plan provided for the grant of ISO, NQSOs, restricted stock and other stock awards

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Table of Contents**EPIX PHARMACEUTICALS, INC.****NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

having such terms and conditions as the compensation committee may determine. Under the 2003 Plan, stock awards were granted to employees and to consultants of the Company. The options were granted at a price not less than fair value of the common stock on the date of grant. At December 31, 2008, shares of common stock are no longer available for grant under the 2003 Plan. The Company assumed options to purchase 1,891,721 shares of Predix common stock as part of the merger. The value of the unvested portion of the options assumed amounted to \$5.4 million and is being recognized as compensation expense over the remaining vesting term of the options.

The Company has recorded \$3.7 million, \$4.8 million and \$4.2 million of stock-based compensation expense, which includes a charge for the shares issued under the Company's Employee Stock Purchase Plan (the ESPP), for the years ended December 31, 2008, 2007 and 2006, respectively. The stock-based compensation expense included \$1.7 million, \$2.5 million and \$2.7 million in research and development and \$2.0 million, \$2.3 million and \$1.5 million in general and administrative expense for the years ended December 31, 2008, 2007 and 2006, respectively. As of December 31, 2008, there was \$5.2 million of unrecognized compensation expense related to non-vested awards that is expected to be recognized over a weighted average period of 2.2 years.

The fair value of each stock option is estimated on the date of grant using the Black-Scholes option pricing model using the assumptions noted in the following table. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected life of the stock options. Expected volatility is based on historical volatility data of the Company's stock and comparable companies to the expected option term. For option grants during 2008, the Company estimated the expected term of options primarily based upon its historical experience of the holding period prior to the exercise or expiration of a vested option. For option grants in 2007 and 2006, the Company utilized the simplified method, as prescribed by the SEC's SAB No. 107, to calculate the expected term.

	<b>Options</b>				<b>ESPP</b>	
	<b>2008</b>	<b>2007</b>	<b>2006</b>	<b>Year Ended December 31, 2008</b>	<b>2007</b>	<b>2006</b>
Expected life of option (years)	5.0	6.3	6.3	0.5	0.5	0.5
Expected stock price volatility	70%	70%	70%	76%	48%	71%
Weighted average risk-free interest rate	3.00%	4.52%	4.69%	1.51%	4.30%	4.93%
Expected annual dividend per share	\$	\$	\$	\$	\$	\$

The weighted-average grant date fair value of stock options granted during 2008, 2007 and 2006 was \$1.57, \$3.69, and \$4.54 per share, respectively. The total intrinsic value of options exercised during 2008, 2007 and 2006 was \$0.1 million, \$1.6 million and \$1.8 million, respectively.

Table of Contents**EPIX PHARMACEUTICALS, INC.****NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

A summary of option activity as of December 31, 2008 and changes during the year then ended is presented below:

	Shares	Weighted - Average Exercise Price	Weighted - Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Outstanding at December 31, 2007	3,847,386	\$ 6.85		
Granted	1,310,496	2.63		
Exercised	(186,215)	0.99		
Cancelled	(1,697,688)	7.43		
Outstanding at December 31, 2008	3,273,979	\$ 5.19	7.29	\$ 17,971
Exercisable at December 31, 2008	1,830,805	\$ 5.85	6.31	\$ 15,399
Vested and expected to vest at December 31, 2008	3,059,209	\$ 5.26	7.19	\$ 17,445

During 2008, the Company granted 173,333 restricted stock units (RSUs) under the 1992 Plan and 2003 Plan, of which 74,876 were forfeited during 2008 and 98,457 remain outstanding as of December 31, 2008. RSUs vest over a two-year period and upon vesting each RSU is exchanged for one share of common stock. No RSUs vested during 2008.

***2006 Employee Stock Purchase Plan***

The Company sponsors the 2006 Employee Stock Purchase Plan (the Purchase Plan) under which employees may purchase shares of common stock at a discount from fair market value at specified dates. Employees purchased 52,815 shares in 2008 at an average price of \$1.39 per share. At December 31, 2008, 92,454 common shares remained available for issuance under the Purchase Plan. The Purchase Plan is intended to qualify as an employee stock purchase plan within the meaning of Section 423 of the Internal Revenue Code of 1986, as amended (the Code). Rights to purchase common stock under the Purchase Plan are granted at the discretion of the compensation committee, which determines the frequency and duration of individual offerings under the Purchase Plan and the dates when stock may be purchased. Eligible employees participate voluntarily and may withdraw from any offering at any time before stock is purchased. Participation terminates automatically upon termination of employment. The purchase price per share of common stock in an offering is 85% of the lesser of its fair market value at the beginning of the offering period or on the applicable exercise date and is paid through payroll deductions.



Table of Contents**EPIX PHARMACEUTICALS, INC.****NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)****10. Income Taxes**

The Company has reported losses since inception and, due to the degree of uncertainty related to the ultimate use of the net operating loss carry forwards, has fully reserved this potential tax benefit. The Company has the following deferred tax assets as of December 31, 2008 and 2007:

	<b>December 31,</b>	
	<b>2008</b>	<b>2007</b>
Deferred tax assets:		
Net operating loss carry forwards	\$ 85,171,000	\$ 65,651,000
Research and development tax credits	3,968,000	1,274,000
Book over tax depreciation and amortization	2,662,000	3,973,000
Deferred revenue	5,542,000	6,301,000
Noncash compensation deductions	1,675,000	1,130,000
Other	785,000	406,000
Total deferred tax assets	99,803,000	78,735,000
Valuation allowance	(99,803,000)	(78,735,000)
Deferred income taxes, net	\$	\$

As of December 31, 2008, the Company had approximately \$215.4 million, \$167.9 million and \$7.5 million of domestic federal, domestic state and foreign net operating loss carry forwards, respectively, which either expire on various dates through 2028 or can be carried forward indefinitely. These loss carry forwards are available to reduce future federal, state and foreign taxable income, if any. The valuation allowance relates to U.S. net operating losses and deferred tax assets and certain other foreign deferred tax assets and is recorded based upon the uncertainty surrounding their realizability, as these assets can only be realized via profitable operations in the respective tax jurisdictions.

As a result of ownership changes resulting from sales of equity securities, the Company's ability to use the operating and acquired net operating loss and credit carry forwards is subject to annual limitations as defined in section 382 and 383 of the Internal Revenue Code. The Company currently estimates that the annual limitation on its use of net operating losses generated through August 15, 2006 will be approximately \$8.5 million through 2011 and approximately \$2.4 million thereafter. The Company also estimates that the annual limitation on its use of acquired net operating losses generated through August 15, 2006 will be approximately \$6.5 million through 2010 and none thereafter. The Company is also eligible for research and development tax credits, which can be carried forward to offset federal taxable income. The annual limitation and the timing of attaining profitability may result in the expiration of net operating loss and tax credit carry forwards before utilization.

In accordance with SFAS No. 109, the accounting for tax benefits of acquired deductible temporary differences and net operating loss carry forwards, which are not recognized at the acquisition date because a valuation allowance is

established and which are recognized subsequent to the acquisition, will be applied first to reduce to zero any goodwill and other non-current intangible assets related to the acquisition. Any remaining benefits would be recognized as a reduction of income tax expense. As of December 31, 2008, \$16.0 million of the Company's deferred tax asset pertains to acquired companies, the future benefits of which will be applied first to reduce to zero any goodwill and other non-current intangible assets related to the acquisitions, prior to reducing income tax expense. Upon adoption of SFAS No. 141-R, *Business Combinations*, prospectively in 2009, the reduction of a valuation allowance that pertains to the acquired companies is generally recorded to reduce the Company's income tax expense.

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The reconciliation of income tax computed at the U.S. federal statutory rate to income tax expense is as follows:

	Years Ended December 31,			Years Ended December 31,		
	2008	2007	2006	2008	2007	2006
Tax at U.S. statutory rate	\$ (12,468,136)	\$ (21,328,352)	\$ (53,464,281)	(34.00)%	(34.00)%	(34.00)%
Permanent differences, net of federal benefit	774,328	832,198	43,305,862	2.11%	1.33%	27.54%
Foreign taxes		58,118	145,313	0.00%	0.09%	0.09%
Operating losses not benefited	11,693,808	20,496,154	10,158,419	31.89%	32.67%	6.46%
Income tax expense	\$	\$ 58,118	\$ 145,313	0.00%	0.09%	0.09%

The Company accounts for its contingencies in accordance with Financial Interpretation Number 48, *Accounting for Uncertain Tax Positions* ( FIN 48 ). FIN 48, which was adopted on January 1, 2007, clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statements in accordance with SFAS No. 109. FIN 48 prescribes a recognition threshold and measurement of a tax position taken or expected to be taken in a tax return. The Company did not establish any reserves for uncertain tax liabilities upon adoption of FIN 48 and has no reserves for uncertain tax positions as of December 31, 2008. The Company will account for interest and penalties related to uncertain tax positions as part of its provision for federal and state income taxes.

The Company is currently open to audit under the statute of limitations by the Internal Revenue Service, state, and foreign jurisdictions for various years from the Company's inception through 2008.

**11. Defined Contribution Plan**

The Company offers a defined contribution 401(k) plan, which covers substantially all US employees. The plan permits participants to make contributions from 1% to 15% of their compensation. The Company matches up to 3% of employees' contributions. During 2008, 2007 and 2006, the Company's match amounted to \$252,686, \$209,704, and \$170,499, respectively.

**12. Strategic Alliances and Collaborations**

The Company's business strategy includes entering into alliances with companies primarily in the pharmaceutical industry to facilitate the development, manufacture, marketing, sale and distribution of EPIX products.

*GlaxoSmithKline*

On December 11, 2006, the Company entered into a development and license agreement with SmithKline Beecham Corporation, doing business as GlaxoSmithKline, and Glaxo Group Limited to develop and commercialize medicines targeting four G-protein coupled receptors, or GPCRs, for the treatment of a variety of diseases, including an option to license the Company's 5-HT<sub>4</sub> partial agonist, PRX-03140. The other three GPCR targets are early discovery programs. PRX-03140 is currently in early-stage clinical development for the treatment of Alzheimer's disease. GlaxoSmithKline does not have options to any of the Company's other clinical programs besides PRX-03140.

Under the terms of the agreement, the Company is obligated to carry out a research and development program for PRX-03140 and three research targets, and to discover and develop compound candidates through proof of concept, typically defined as the completion of Phase 2 clinical studies. Upon completion of the proof of concept package for each of these four programs, GlaxoSmithKline has the exclusive option, exercisable at GlaxoSmithKline's sole discretion, to obtain exclusive, worldwide license rights to complete the development



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**EPIX PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

and to commercialize products based on such compound. The research term, which began on December 11, 2006, continues for a minimum of six years and may be extended to December 11, 2020. During the research term, the Company is obligated to participate on a joint steering committee comprised of members from GlaxoSmithKline and the Company, which oversees the collaboration. At the end of the research term, the Company can elect at any time to withdraw from participation in the joint steering committee, or other committees established under the agreement. In connection with a workforce reduction implemented in March 2009, the Company entered into a letter agreement with GlaxoSmithKline allowing the Company to reduce its research and development obligations under the development and license agreement, during the period from March 13, 2009 to September 13, 2009, for programs other than the PRX-03140 program.

In return for the exclusive options described above and in consideration of the development work to be performed by the Company under the collaboration agreement, GlaxoSmithKline paid the Company an initial payment of \$17.5 million. The Company also entered into a stock purchase agreement with GlaxoSmithKline providing for the issuance and sale to GlaxoSmithKline of 3,009,027 shares of the Company's common stock for an aggregate purchase price of \$17.5 million, which represented the fair value of the Company's common stock at the time of purchase.

The Company is recognizing the initial payment of \$17.5 million as revenue ratably over the fourteen-year maximum research term from December 11, 2006 through December 11, 2020. The Company has no substantive obligations to GlaxoSmithKline upon the expiration of the research term. The Company has recognized \$2.6 million of the \$17.5 million as revenue from inception of the contract through December 31, 2008.

The Company may be eligible for up to an aggregate of \$1.2 billion in additional nonrefundable option fees and milestone payments that relate to the achievement of certain development, regulatory and commercial milestones across the four research programs. As the option fees and milestone payments represent significant performance risks, the Company recognizes the payments as revenue when the performance obligations, as defined in the contract, are achieved. The Company has recognized \$19.0 million of revenue for milestone payments received from inception of the contract through December 31, 2008. In addition, GlaxoSmithKline is obligated to reimburse the Company for certain clinical and discovery costs across all four research programs. The Company recognizes the reimbursement of such research and development costs by GlaxoSmithKline as revenue as the related costs are incurred in accordance with EITF Issue No. 99-19 *Reporting Revenue Gross as a Principal Versus Net as an Agent*. The Company has recognized \$8.1 million in revenue from inception of the contract through December 31, 2008 associated with cost reimbursements from GlaxoSmithKline.

The Company is also eligible to receive tiered, double-digit royalties based on net sales by GlaxoSmithKline of any products developed under the collaboration agreement. The specific royalty rates will vary depending upon a number of factors, including the total annual net sales of the product and whether it is covered by one of the Company's patents. GlaxoSmithKline's royalty obligation under the collaboration agreement generally terminates on a product-by-product and country-by-country basis upon the later of (i) the expiration of the Company's last patent claiming the manufacture, use, sale or importation of the product in the relevant country and (ii) twelve years after the first commercial sale of the product in the relevant country. Royalties, if any, will be recognized as revenue when earned, are reasonably estimable and collection is probable, which is typically upon receipt of royalty reports from the licensee or cash. Although the Company is eligible for milestone payments, option fees and royalty payments under the collaboration agreement, it does not expect any such payments will extend its available cash beyond the end of August 2009.

If GlaxoSmithKline does not exercise any of the four options, the collaboration agreement will expire upon the expiration of the last such option. Otherwise, the collaboration agreement will expire on a product-by-product and country-by-country basis upon the expiration of the royalty payment obligations for each product in each country.

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**EPIX PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

The Company has retained an option to co-promote products successfully developed from the 5-HT4 program in the United States. Under any such co-promotion arrangement, the collaboration agreement provides for GlaxoSmithKline to direct the promotional strategy and compensate the Company for its efforts in co-promoting the product.

The Company has responsibility and control for filing, prosecution or maintenance of any of its patents that are the subject of an option to GlaxoSmithKline under the collaboration agreement, provided that in the event an option is exercised, responsibility and control of the patents subject to such option transfers to GlaxoSmithKline.

The parties each have the right to terminate the collaboration agreement if the other party becomes insolvent or commits an uncured material breach of the collaboration agreement. In addition, GlaxoSmithKline has the right to terminate the collaboration agreement in its entirety, and to terminate its rights to any program developed under the collaboration agreement on a regional or worldwide basis, in each case without cause. Upon a termination of the collaboration agreement, depending upon the circumstances, the parties have varying rights and obligations with respect to the grant of continuing license rights, continued commercialization rights and continuing royalty obligations.

***Amgen***

As part of the Predix merger, the Company assumed an obligation for an exclusive license agreement with Amgen Inc., entered into on July 31, 2006, to develop and commercialize products based on the Company's 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. The S1P1 receptor is a cell surface GPCR found on white blood cells and in other tissues that is associated with certain autoimmune diseases, such as rheumatoid arthritis and multiple sclerosis.

Pursuant to the license agreement, the Company granted Amgen an exclusive worldwide license to its intellectual property and know-how related to the compounds in the Company's S1P1 program that modulate the S1P1 receptor, for the development and commercialization of those compounds and other compounds and products that modulate the S1P1 receptor. Amgen has limited rights to sublicense its rights under the license. In return for the license, Amgen paid the Company a nonrefundable, up-front payment of \$20.0 million and will pay royalties based on aggregate annual net sales of all S1P1-receptor-modulating products developed by Amgen under the license agreement. In addition, the Company may be eligible for up to an aggregate of \$287.5 million of nonrefundable milestone payments that relate to milestones associated with the commencement of clinical trials, regulatory approvals and annual net sales thresholds of the products under the license agreement. These royalty rates and milestone amounts are subject to reduction in the event that, among other things:

Amgen is required to obtain third-party rights to develop and commercialize a product that incorporates an EPIX compound; and

Amgen develops and commercializes products that are not covered by the intellectual property rights the Company licensed to Amgen, such as for example, S1P1-modulating products that may be acquired by Amgen from a third-party.

Although the Company is eligible for milestone payments and royalty payments under the agreement, it does not expect any such payments will extend its available cash beyond the end of August 2009.

Generally, Amgen's royalty obligation under the agreement terminates on a product-by-product and country-by-country basis upon the later of (a) the expiration or termination of the last claim within the patents (whether such patents are patents EPIX licensed to Amgen or are patents owned or in-licensed by Amgen)

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**EPIX PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

covering such product and (b) ten years following the first commercial sale of the product. The agreement expires when all of Amgen's royalty obligations have terminated.

The Company has the option to co-promote one product from the collaboration in the United States for one indication to be jointly selected by EPIX and Amgen. During the first 15 months of the agreement, the Company was required to design, discover and develop, at its own cost, additional compounds that modulate the S1P1 receptor and that are within the same family of compounds as those identified in its patent applications licensed to Amgen under the agreement. The collaboration agreement provides Amgen with a license to these additional compounds to further its development efforts. The Company may undertake additional research under the agreement, at its own expense, as approved by a joint steering committee formed pursuant to the agreement. The Company had responsibility and control for filing, prosecution or maintenance for any of its patents licensed to Amgen for 24 months, at which time, responsibility and control of such patents transferred to Amgen. Amgen now has responsibility and control for filing, prosecution or maintenance for all patents covered by the agreement, including patents jointly developed under the agreement. Amgen will have final decision making authority on all other research matters and will be responsible for non-clinical and clinical development, manufacturing, regulatory activities and commercialization of the compounds and products developed under the license agreement, at its own expense.

The parties each have the right to terminate the agreement (in whole or for specified products or countries, depending upon the circumstances) upon a material uncured breach by the other party and Amgen has the right to terminate the agreement for convenience upon varying periods of at least three months advance notice. Upon a termination of the agreement, depending upon the circumstances, the parties have varying rights and obligations with respect to the grant of continuing license rights, continued commercialization rights and continuing royalty obligations.

***Cystic Fibrosis Foundation Therapeutics, Incorporated***

On April 1, 2008, the Company entered into a new Research, Development and Commercialization Agreement (the Agreement) with Cystic Fibrosis Foundation Therapeutics, Incorporated (CFFT), the drug discovery and development affiliate of the Cystic Fibrosis Foundation. The Agreement provides for the continuation of the first research program initiated under a prior Research, Development and Commercialization Agreement between Predix and CFFT dated March 7, 2005, as amended. Under the Agreement, the Company has agreed to conduct additional research activities aimed at developing a compound to correct a malfunction of the cystic fibrosis transmembrane conductance regulator protein. CFFT may make payments of up to \$30.7 million under the Agreement for research services and reimbursed research costs. The Company may also be eligible to receive up to an additional \$7.0 million for the achievement of certain development milestones. The Company does not currently expect that any payments for which it may be eligible from CFFT will materially supplement its cash position prior to the end of August 2009, if at all. The Company recognizes the reimbursement of such research and development costs by CFFT as revenue as the related costs are incurred in accordance with EITF Issue No. 99-19 *Reporting Revenue Gross as a Principal Versus Net as an Agent*. The Company has recognized, from August 16, 2006 (date of the Predix merger) through December 31, 2008, \$7.0 million in revenue associated with cost reimbursements and \$2.3 million from milestones earned from CFFT.

Upon any commercialization by the Company of a product developed under the Agreement, the Company is required to pay tiered royalties to CFFT based on net sales by the Company of such product. In addition, the Company is required to make certain payments to CFFT if the Company outlicenses a product developed under the Agreement.

The research program is scheduled to conclude on April 1, 2017, but can be extended for up to three additional years if the Company is conducting a certain clinical trial, or by agreement of the parties. The Agreement terminates at such time when there are no longer any royalty payment obligations owing under the

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**EPIX PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

Agreement. Upon an earlier termination of the Agreement by either party, depending upon the circumstances, the parties have varying rights and obligations with respect to intellectual property rights and payment obligations.

***Bayer Schering Pharma AG, Germany***

In September 2008, Bayer Schering Pharma AG, Germany (Bayer Schering), terminated the Amended and Restated Strategic Collaboration Agreement by and between the Company and Bayer Schering, dated as of June 9, 2000 and amended as of December 22, 2000 (the Agreement), effective March 1, 2009. Accordingly, the worldwide commercial rights for the Company's blood pool magnetic resonance angiography agent, Vasovist, were transferred back to the Company on such date.

Under the Agreement, the Company granted Bayer Schering an exclusive license to co-develop and market Vasovist worldwide. Generally, each party to the Agreement shared equally in Vasovist development costs. Pursuant to the terms of the Agreement, the Company retained responsibility for completing clinical trials and filing for U.S. Food and Drug Administration approval in the United States, and Bayer Schering retained responsibility for clinical and regulatory activities for Vasovist outside the United States. In addition, the Company was entitled to receive a royalty on products sold outside the United States and a percentage of Bayer Schering's operating profit margin on products sold in the United States.

Bayer Schering had the right to terminate the Agreement at any time on a region-by-region basis or in its entirety, upon six months written notice to the Company, which right was exercised as described above. Upon termination of the Agreement, all patent rights granted to Bayer Schering terminated and Bayer Schering was required to grant the Company an exclusive, worldwide royalty bearing license for any related patent rights owned by Bayer Schering. In addition, if the Company subsequently enters into a collaboration agreement with a third party for the commercialization of Vasovist, which is the Company's current intention, the Company will be required under the Agreement to reimburse Bayer Schering for a portion of their development costs. The reimbursement will be based on pre-defined percentages of the development costs, allocated to each territory for which the commercial rights are sold, with full worldwide rights amounting to a \$33 million reimbursement to Bayer Schering.

In May 2003, the Company entered into a broad alliance with Bayer Schering for the discovery, development and commercialization of molecularly-targeted contrast agents for MRI. The alliance was composed of two areas of collaboration, with one agreement generally providing for exclusive development and commercialization collaboration for EP-2104R, the Company's product candidate for the detection of thrombus, and the second agreement covering an exclusive research collaboration to discover novel compounds for diagnosing human disease using MRI. Under the first agreement, Bayer Schering had an option to the late stage development and worldwide marketing rights for EP-2104R. In July 2006, Bayer Schering notified the Company that it declined to exercise this option. As a result, the Company retained commercial rights to EP-2104R. In the event EP-2104R is commercialized, the Company is obligated to pay Bayer Schering a minimal royalty limited to a portion of the funding the Company received for this program from Bayer Schering. The second agreement related to the broader research collaboration concluded in May 2006.

On May 8, 2000, the Company granted to Bayer Schering a worldwide, royalty-bearing license to patents covering Bayer Schering's development project, Primovist, an MRI contrast agent for imaging the liver, which was approved in the European Union in 2004. Under this agreement, Bayer Schering is required to pay the Company royalties based on

sales of products covered by this agreement. To date, the Company has not received any material royalties from Bayer Schering under this agreement, and does not expect any for the foreseeable future. This agreement expires upon the last-to-expire patent covered by the agreement unless terminated earlier by either party because of the material breach of the agreement by the other party.



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**EPIX PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

**Technology Agreements**

***Ramot***

The Company's proprietary drug discovery technology and approach is in part embodied in technology that it licenses from Ramot at Tel Aviv University Ltd., the technology transfer company of Tel Aviv University. Pursuant to this license, the Company has exclusive, worldwide rights to certain technology developed at Tel Aviv University to develop, commercialize and sell products for the treatment of diseases or conditions in humans and animals. The licensed technology, as continually modified, added to and enhanced by the Company, consists in large part of computer-based models of biological receptors and methods of designing drugs to bind to those receptors.

All of the Company's 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, and the Company would be required to make payments to Ramot, as described below, as and when rights to any such drug candidates are ever sublicensed or any such drug candidates are commercialized. In addition, the Company has used the licensed technology in all of its preclinical-stage programs and would expect to make payments to Ramot if rights to any drug candidates were ever commercialized from any of these programs. One of our employees, Sharon Shacham, Senior Vice President of Drug Development, was an inventor of the technology that the Company licenses from Ramot. The Company believes that Ramot shares a portion of any royalty income received with the respective inventors and, accordingly, Dr. Shacham receives a portion of the amounts the Company pays Ramot.

The Company paid Ramot an upfront fee of \$40,000 upon the grant of the license. Under the license, the Company has an obligation to make royalty payments to Ramot on the Company's net sales of products that are identified, characterized or developed through the use of the licensed technology that are either 1.5% or 2.5% of such net sales (depending upon the degree to which the product needed to be modified after being identified, characterized or developed through the use of the licensed technology) and decrease as the volume of sales increases. The royalty obligation for each product expires on a country-by-country basis twelve years after the first commercial sale. There is also an annual minimum royalty payment obligation of \$10,000 per year.

The Company also is required to share between 5% and 10% of the consideration it receives from parties to whom it grants sublicenses of rights in the Ramot technology or sublicenses of rights in products identified, characterized or developed with the use of such technology and between 2% and 4% of consideration the Company receives from performing services using such technology. In connection with the Company's collaborations with CFFT, Amgen and GlaxoSmithKline, the Company has paid approximately \$3.3 million in royalties to Ramot primarily for payments received to date for the upfront license fees and milestone payments received under these license agreements.

The license may be terminated by either party upon a material breach by the other party unless cured within 30 days, in the case of a payment breach, and 90 days in the case of any other breach. The license may also be terminated by either party in connection with the bankruptcy or insolvency of the other party. The license expires upon the expiration of the Company's obligation to make payments to Ramot. Therefore, since the Company has an ongoing obligation to pay annual minimum royalties to Ramot as described above, the license may not expire and may only terminate upon a breach by, or bankruptcy of, a party.

***Covidien Ltd.***

In August 1996, the Company entered into a strategic collaboration agreement with Mallinckrodt Inc. (subsequently acquired by Covidien Ltd.), involving research, development and marketing of MRI vascular contrast agents developed or in-licensed by either party. In June 2000, in connection with the exclusive license that the Company granted to Bayer Schering under its strategic collaboration agreement, the Company

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**EPIX PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

amended its strategic collaboration with Covidien. The amendment enabled the Company to sublicense certain technology from Covidien to Bayer Schering which allowed the Company to enter into the strategic collaboration agreement for Vasovist with Bayer Schering. Pursuant to that amendment, the Company also granted to Covidien a non-exclusive, worldwide license to manufacture Vasovist for clinical development and commercial use on behalf of Bayer Schering in accordance with a manufacturing agreement entered into in June 2000 between Covidien and Bayer Schering. In connection with this amendment, the Company paid Covidien an up-front fee of \$10.0 million and was obligated to pay up to an additional \$5.0 million in milestone payments, of which \$2.5 million was paid following NDA filing in February 2004 and \$2.5 million was recognized as a royalty expense upon marketing approval in the United States in December 2008 and was paid to Covidien in January 2009. The Company is also obligated to pay Covidien a share of its Vasovist operating profit margins in the United States and a percentage of any royalty that the Company receives on Vasovist gross profits outside the United States.

As a result of the termination of the Company's strategic collaboration agreement with Bayer Schering effective March 1, 2009, Bayer Schering is required to assign to the Company certain rights and obligations under the June 2000 manufacturing agreement between Bayer Schering and Covidien. The Company is currently in discussions with Covidien regarding such assignment. Covidien is currently the only entity approved by the FDA to manufacture Vasovist.

***Massachusetts General Hospital***

In July 1995, the Company entered into a license agreement with MGH pursuant to which MGH granted the Company an exclusive worldwide license to patents and patent applications which relate to Vasovist. The MGH license requires the Company to pay royalties on the net sales of products covered by this license, including Primovist, MultiHance and Vasovist. The Company has paid MGH approximately \$0.7 million in royalty payments through December 31, 2008 under this license agreement. The license agreement expires on a country-by-country basis when the patents covered by the license agreement expire. The license agreement does not contain a renewal provision. The Company believes that the expiration of these patents does not compromise its proprietary position with respect to Vasovist because Vasovist is covered by composition of matter patents independent of its license with MGH. These composition of matter patents extend into 2015 in the United States, although the life of these patents may be extended.

**13. Subsequent Event (unaudited)**

On March 12, 2009, the Company initiated a cost reduction initiative by reducing its workforce by approximately 44 full-time equivalent positions, representing approximately 50% of the Company's workforce, effective immediately. The Company expects to incur a charge of approximately \$0.6 million in the first quarter of 2009 for employee termination benefits, including severance and other benefits. The Company expects this workforce reduction to reduce its annual salary and benefit costs by approximately \$4.4 million.

**Table of Contents****EPIX PHARMACEUTICALS, INC.****NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)****14. Quarterly Financial Information (unaudited)**

The tables below set forth unaudited quarterly financial data for each of the last two years:

	<b>March 31, 2008</b>	<b>June 30, 2008</b>	<b>September 30, 2008</b>	<b>December 31, 2008</b>
Revenues:				
Product development revenue	\$ 1,927,420	\$ 16,868,438	\$ 4,500,280	\$ 2,894,065
Royalty revenue	137,844	159,196	159,711	169,477
License fee revenue	343,010	327,361	440,829	700,724
Total revenues	2,408,274	17,354,995	5,100,820	3,764,266
Operating expenses:				
Research and development	12,691,249	15,041,755	10,954,028	7,554,107
General and administrative	3,038,260	3,356,021	3,580,761	3,048,659
Royalties	39,046	694,434	70,241	2,558,027
Restructuring				242,445
Total operating expenses	15,768,555	19,092,210	14,605,030	13,403,238
Operating loss	(13,360,281)	(1,737,215)	(9,504,210)	(9,638,972)
Interest and other income	629,225	288,291	257,537	179,284
Interest expense	(1,003,430)	(887,040)	(943,970)	(950,208)
Loss before provision for income taxes	(13,734,486)	(2,335,964)	(10,190,643)	(10,409,896)
Provision for income taxes				
Net loss	\$ (13,734,486)	\$ (2,335,964)	\$ (10,190,643)	\$ (10,409,896)
Weighted average shares, basic and diluted	41,353,992	41,358,087	41,473,368	41,679,996
Net loss per share:				
Basic and diluted	\$ (0.33)	\$ (0.06)	\$ (0.25)	\$ (0.25)

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	<b>March 31, 2007</b>	<b>June 30, 2007</b>	<b>September 30, 2007</b>	<b>December 31, 2007</b>
Revenues:				
Product development revenue	\$ 434,392	\$ 395,087	\$ 4,192,766	\$ 5,216,875
Royalty revenue	487,658	315,135	100,470	114,406
License fee revenue	1,032,850	1,046,458	1,046,459	577,493
Total revenues	1,954,900	1,756,680	5,339,695	5,908,774
Operating expenses:				
Research and development	13,491,119	14,789,943	14,930,082	14,315,362
General and administrative	8,613,758	4,478,387	3,560,010	3,399,738
Royalties	53,668	83,428	203,475	254,698
Restructuring		350,137		
Total operating expenses	22,158,545	19,701,895	18,693,567	17,969,798
Operating loss	(20,203,645)	(17,945,215)	(13,353,872)	(12,061,024)
Interest and other income	1,962,953	1,174,354	927,549	836,250
Interest expense	(1,230,734)	(1,252,945)	(504,397)	(1,079,719)
Loss before provision for income taxes	(19,471,426)	(18,023,806)	(12,930,720)	(12,304,493)
Provision for income taxes	38,089	20,029		
Net loss	\$ (19,509,515)	\$ (18,043,835)	\$ (12,930,720)	\$ (12,304,493)
Weighted average shares, basic and diluted	32,586,377	32,622,318	32,850,191	37,686,382
Net loss per share:				
Basic and diluted	\$ (0.60)	\$ (0.55)	\$ (0.39)	\$ (0.33)