EPIX Pharmaceuticals, Inc.
Form S-1
December 03, 2007

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As filed with the Securities and Exchange Commission on December 3, 2007
Registration No. 333-

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

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

EPIX PHARMACEUTICALS, INC.
(Exact Name of Registrant as Specified in Its Charter)

Delaware	**2835**	**04-3030815**
(State of Incorporation)	*(Primary Standard Industrial Classification Code Number)*	*(I.R.S. Employer Identification Number)*

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

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

Copy to:

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

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

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. þ

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

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

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

Title of Each Class of Securities to be Registered	Amount to be Registered(1)	Proposed Maximum Offering Price per Unit (2)	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee
Common Stock, par value $.01 per share	5,245,468	$3.01	$15,788,859	$484.72

(1) This registration statement shall also cover any additional shares of common stock which become issuable by reason of any stock dividend, stock split, recapitalization or any other similar transaction effected without the receipt of consideration which results in an increase in the number of the registrant s outstanding shares of common stock.

(2) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(c) of the Securities Act of 1933. The price per share is based on the average of the high and low sale prices of the common stock on November 26, 2007, as reported on the NASDAQ Global Market.

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

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

SUBJECT TO COMPLETION, DATED DECEMBER 3, 2007

PROSPECTUS

5,245,468 Shares

Common Stock

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

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

Our common stock is listed on the NASDAQ Global Market under the symbol EPIX. On November 30, 2007, the last reported sale price of our common stock on the NASDAQ Global Market was $3.18 per share.

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

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

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

The date of this prospectus is December 3, 2007.

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

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PROSPECTUS SUMMARY

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

Overview

We are a biopharmaceutical company focused on discovering, developing and commercializing novel pharmaceutical products through the use of proprietary technologies to better diagnose, treat and manage patients. We have four internally discovered therapeutic product candidates in clinical trials. These drug candidates are targeting conditions such as depression, Alzheimer s disease, cardiovascular disease, cognitive impairment and obesity. Our blood-pool imaging agent, Vasovist is approved for marketing in more than 30 countries outside of the United States. We also have collaborations with SmithKline Beecham Corporation, or GlaxoSmithKline, Amgen Inc., Cystic Fibrosis Foundation Therapeutics Incorporated, and Bayer Schering Pharma AG, Germany (formerly known as Schering AG).

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

Our Product Candidates

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

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Risks Affecting Us

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

- a substantial portion of our future revenues will be dependent upon our agreements with GlaxoSmithKline, Amgen Inc., Bayer Schering Pharma AG, Germany and other third-parties with whom we may in the future enter into a collaboration;
- we anticipate future losses and may never become profitable; and
- we have never had a commercially available product in the United States and we may never succeed in developing marketable products.

Recent Developments

On November 15, 2007, we issued and sold in a private placement an aggregate of 5,245,468 shares of our common stock at a purchase price of $3.10 per share. This private placement resulted in gross proceeds to us of approximately $16.3 million, which, after payment of expenses of the private placement, will be used to finance ongoing clinical trials, advance our research and development activities and fund general corporate operations. In connection with the private placement, we have granted registration rights for the shares of our common stock received by the selling stockholders. See discussion of the registration rights discussed under the section Registration Rights on page 28.

Corporate Information

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

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RISK FACTORS

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

Risks Related to Our Business

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

We expect that a substantial portion of our future revenues will be dependent upon our collaboration agreements with GlaxoSmithKline and with Amgen Inc. The agreement with GlaxoSmithKline encompasses the development and commercialization of medicines targeting four G-protein coupled receptors, or GPCRs, for the treatment of a variety of diseases, including an option to license our 5-HT4 partial agonist, PRX-03140, and other medicines arising from the four research programs. The agreement with Amgen encompasses the development and commercialization of products based on our pre-clinical compounds that modulate the S1P1 receptor and compounds and products that may be identified by or acquired by Amgen and that modulate the S1P1 receptor. We are substantially dependent upon Bayer Schering Pharma AG, Germany to commercialize Vasovist, our lead imaging product candidate, in the United States and Europe. If these collaborators were to terminate their agreements with us, fail to meet their obligations or otherwise decrease their commitment there under, our future revenues could be materially adversely affected and the development and commercialization of our product candidates would be interrupted. In addition, if we do not achieve some or any of the development, regulatory and commercial milestones or if GlaxoSmithKline or Amgen does not achieve certain net sales thresholds, in each case, as set forth in the respective agreements, we will not fully realize the expected benefits of the agreements. Further, the achievement of certain of the various milestones under our collaboration agreements with GlaxoSmithKline, Amgen and Bayer Schering Pharma AG, Germany will depend on factors that are outside of our control and most are not expected for several years, if at all. Moreover, our receipt of revenues under our agreements with these collaborators will be directly affected by the level of efforts of such collaborators and we cannot control whether they will devote sufficient resources to development or commercialization of the technology under their respective agreement or whether they will elect to pursue the development or commercialization of alternative products or services. For instance, Bayer Schering Pharma AG, Germany currently markets imaging agents for other technologies that will compete against Vasovist, and Bayer Schering Pharma AG, Germany will be responsible for setting the price of the product candidate worldwide. Accordingly, Bayer Schering Pharma AG, Germany may not set prices in a manner that maximizes revenues for us. Disagreements with our collaborators could delay or terminate the continued development and commercialization of the licensed products under our agreements or result in litigation, either of which could have a material adverse affect on our business, financial condition and results of operations overall. In addition, Bayer Schering Pharma was recently formed through the merger of Bayer AG and Schering AG. If the strategy of Bayer Schering Pharma AG, Germany differs from that of Schering AG s prior strategy with respect to the marketing of Vasovist, our expectations regarding the marketing of Vasovist could be negatively impacted, which could have a material adverse effect on our imaging business. If any of our agreements with GlaxoSmithKline, Amgen or Bayer Schering Pharma AG, Germany is terminated prior to expiration, we would be required to enter into other strategic relationships or find alternative ways of continuing our product development programs. We cannot assure you that we would be able to enter into similar agreements with other companies with sufficient product development capabilities to commercialize our product

candidates, and our failure to do so could materially and adversely affect our ability to generate revenues.

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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 September 30, 2007 were approximately $396.0 million. These losses have primarily resulted from expenses associated with our research and development activities, including pre-clinical 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, pre-clinical 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 product candidates, which trials would be expensive and which could contribute to our continuing to incur losses.

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

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 has 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 restrospectively selected grant dates for certain grants awarded between February 1997 and February 2004, covering options to purchase approximately 1.4 million shares of our common stock, differed from the measurement dates previously used for such stock awards. In addition, we determined that certain of our former senior management re-priced, as defined by financial accounting standards, approximately 0.9 million stock options awarded during the period between June 1999 and March 2005, and we identified approximately 0.1 million options in which other dating errors resulted in stock options with grant dates that failed to meet the measurement date criteria of APB 25. As a result, we applied revised measurement dates to the option grants with administrative errors and option grants for which certain of our former senior management retrospectively selected grant dates, and, for options that were re-priced, as defined by financial accounting standards, we revised our accounting for such re-priced awards from accounting for the grants as fixed awards to accounting for the grants as variable awards. As a result of these adjustments, 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. In addition, we have accrued payroll tax expense of approximately $0.9 million relating to employer and employee payroll taxes, interest and penalties we estimate we will owe as a result of the modifications to exercised options previously considered incentive stock options that should have been taxed as non-qualified stock options. Our historical stock option practices and the restatement of our prior financial statements expose us to greater risks associated with litigation and regulatory proceedings. The Securities and Exchange Commission has advised us that it has commenced an informal investigation regarding our stock option grants. We are cooperating with that investigation. In the event of any litigation or regulatory proceeding involving a finding or assertion by the Securities and Exchange Commission, other federal or state governmental agencies, or any third-party that our past stock option practices violated the federal securities laws or other laws, we may be required to pay fines, penalties or other amounts, may be subject to other remedies or remedial actions, and/or may be required to further restate prior period financial statements or adjust current period financial statements. In addition, considerable legal and accounting expenses related to these matters have been incurred to date and significant expenditures may continue to be incurred in the future.

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

Vasovist has not been approved for marketing and sale in the United States by the FDA. In connection with a new drug application, or NDA, that we submitted for Vasovist in December 2003, we received an approvable letter from the FDA in January 2005 in which the FDA requested additional clinical trials prior to approval. In May 2005, we submitted a response to the FDA approvable letter, which was accepted by the FDA as a complete response in June 2005. In November 2005, the FDA provided us with a second approvable letter which indicated that at least one additional clinical trial and a re-read of images obtained in certain previously completed Phase 3 trials will be necessary before the FDA could approve Vasovist. We believe that these trials would require a substantial period of time to complete. We have had three meetings with the FDA since receiving the second approvable letter to discuss the path forward for Vasovist in the United States. After considering the parameters of the additional clinical trials requested by the FDA, we filed a formal appeal with the FDA asking the FDA to approve Vasovist and to utilize an advisory committee as part of the appeal process. In August 2006, the FDA denied our appeal and suggested that we conduct two new clinical trials for Vasovist. In February 2007, we filed our second formal appeal with the FDA asking the FDA to approve Vasovist and to utilize an advisory committee as part of the appeal process. On June 15, 2007, we received a letter from the FDA denying our second formal appeal, but indicated that a blinded re-read, or reanalysis, of the images obtained in our previously completed Phase 3 clinical trials of Vasovist could provide the potential core of the evidence to support approval of Vasovist if the results of the re-read are positive and that further clinical trials may not be necessary. We are currently in discussions with the FDA regarding the development of appropriate protocol for the re-read, including how the reading will be done, how the data from the re-reading will be analyzed and a plan for statistical analysis, prior to conducting a re-read of the images. The approval, timeliness of approval and labeling of Vasovist are subject to significant uncertainties related to a number of factors, including:

- the process of reaching agreement with the FDA on the protocols required for a re-read of the images obtained from the completed Phase 3 trials;
- obtaining the desired results of such re-read of images by a new group of radiologists; and
- the FDA s review process and conclusions regarding any additional Vasovist regulatory submissions.

We cannot assure you that the blinded re-read process will be successful or that we will be able to reach agreement with the FDA on the design or clinical endpoints for a blinded re-read of images from the completed Phase 3 trials. Further, we cannot assure you that any such agreed upon protocol for a re-read will be feasible for us to conduct or whether such re-read will be completed in a commercially reasonable timeframe, if at all. If the FDA does not approve Vasovist, then we will not receive revenues based on sales of Vasovist in the United States. Even if ultimately approved, we do not expect revenues from the commercial sales of any of our product candidates, other than Vasovist, for at least several years.

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

We have never had any product candidates receive regulatory approval for commercial sale in the United States and do not expect to have any commercial therapeutic products available in the United States for at least the next several years, if at all. In September 2006, results from our pivotal Phase 3 clinical trial of our PRX-00023 product candidate for generalized anxiety disorder demonstrated that PRX-00023 did not achieve a statistically significant improvement over placebo for the primary endpoint with respect to generalized anxiety disorder. Prior to obtaining results from this trial, PRX-00023 was our most advanced therapeutic drug candidate. Based on these trial results, however, we have discontinued our development efforts with respect to PRX-00023 in anxiety and currently are focusing our

development efforts for this product candidate in depression. PRX-00023 has not been tested in patients with a primary diagnosis of major depression and will require significant further additional clinical testing for that indication. In addition, although our Vasovist imaging product has been approved for commercial sale in more than 30 countries outside of the United States, and is currently being marketed in Europe by Bayer Schering Pharma AG, Germany, we have not obtained approval of Vasovist in the United States and do not expect any significant income or royalties as a result of sales of

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Vasovist for the foreseeable future., The approval of Vasovist by the FDA is subject to significant uncertainty and we may never obtain regulatory approval to market Vasovist in the United States.

In addition to PRX-00023 and Vasovist, each of our other clinical-stage drug candidates in the United States require additional clinical studies: PRX-08066 for the treatment of two types of pulmonary hypertension pulmonary hypertension associated with chronic obstructive pulmonary disease, which will began a Phase 2b clinical trial in the first quarter of 2008, and pulmonary arterial hypertension; PRX-03140 for the treatment of Alzheimer s disease, which entered a Phase 2 clinical trial in the fourth quarter of 2006; PRX-07034 for the treatment of obesity and cognitive impairment, which will commence a Phase 2 clinical trial in the first half of 2008. Prior to the initiation of our Phase 2 clinical trial, PRX-08066 had never been tested in patients with pulmonary hypertension associated with chronic obstructive pulmonary disease and has never been tested in patients with primary pulmonary arterial hypertension. PRX-07034 is currently being tested in patients with obesity and has never been tested in patients with cognitive impairment. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in early-stage clinical development. For example, Sanofi-Aventis discontinued the development of its product candidate for the treatment of Alzheimer s disease designed to target the 5-HT4 protein receptor due to lack of efficacy. This compound is believed to have the same mechanism of action as PRX-03140, was more advanced in clinical development and was more potent in 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.

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

- our failure to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for a particular indication;
- our inability to demonstrate that a product candidate s benefits outweigh its risks;
- our inability to demonstrate that the product candidate presents a significant advantage over existing therapies;
- the FDA s or comparable foreign regulatory authorities disagreement with the manner in which we and our collaborators interpret the data from pre-clinical 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.

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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 3 clinical trial of PRX-00023 in generalized anxiety disorder, which was designed to evaluate the efficacy of PRX-00023 as measured by the change from baseline in the Hamilton Rating Scale for Anxiety compared to placebo, demonstrated that PRX-00023 did not achieve a statistically significant improvement over placebo for the primary endpoint with respect to generalized anxiety disorder. Based on these results, we have discontinued our development efforts of PRX-00023 in anxiety. We have limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals for our product candidates, including filing and prosecuting the applications necessary to gain approval by the FDA. Our NDA for Vasovist has not been, and may never be, approved by the FDA and we have not submitted an NDA to the FDA for any of our other product candidates. This limited experience may result in longer regulatory processes in connection with our efforts to obtain approval of our product candidates. With respect to both our current product candidates in human clinical trials and our research product candidates which may be suitable for testing in human clinical trials at some point in the future, we face risks including that:

- the product candidate may not prove to be safe and efficacious;
- the dosage form of the product candidate may not deliver reproducible amounts of product to patients;
- patients may die or suffer other adverse effects for reasons that may or may not be related to the product candidate being tested;
- the results of later-stage clinical trials may not confirm the positive results of earlier trials;
- the results may not meet the level of statistical significance required by the FDA or other regulatory agencies for approval; and
- the FDA or other regulatory agencies may require additional or expanded trials.

Of the large number of product candidates in development, only a small percentage result in the submission of an NDA to the FDA and even fewer are approved for commercialization. If we fail to demonstrate the safety and efficacy of our product candidates, we will not be able to obtain the required regulatory approvals to commercialize these

product candidates. The results from pre-clinical testing of a product candidate that is under development may not be predictive of results that will be obtained in human clinical trials. In addition, the results of early human clinical trials may not be predictive of results that will be obtained in larger scale, advanced-stage clinical trials. Our current product candidates and any other product candidates we may seek to develop in the future may never complete the clinical testing necessary to obtain the appropriate regulatory approvals for us to begin selling them.

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

We may encounter problems with our completed, ongoing or planned clinical trials for our product candidates that will cause us or any regulatory authority to delay or suspend those clinical trials or delay the analysis of data derived from them. A number of events, including any of the following, could delay the completion of our ongoing and planned clinical trials for our product candidates and negatively impact our ability to obtain regulatory approval or enter into collaborations for, or market or sell, a particular product candidate, including any of our current clinical-stage product candidates:

- conditions imposed on us by the FDA or any foreign regulatory authority regarding the scope or design of our clinical trials;
- delays in obtaining, or our inability to obtain, required approvals from institutional review boards or other reviewing entities at clinical sites selected for participation in our clinical trials;
- delay in developing a clinical dosage form, insufficient supply or deficient quality of our product candidates or other materials necessary to conduct our clinical trials;
- negative or inconclusive results from clinical trials, or results that are inconsistent with earlier results, that necessitate additional clinical study;
- serious and/or unexpected product-related side effects experienced by subjects in clinical trials; or
- failure of our third-party contractors or our investigators to comply with regulatory requirements or otherwise meet their contractual obligations to us in a timely manner.

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

In addition, the number and complexity of clinical trials needed to achieve regulatory approval for our therapeutic drug candidates, including but not limited to PRX-00023, our product candidate for the treatment of depression, and PRX-03140, our product candidate for the treatment of Alzheimer s disease, could be significant. Achieving primary efficacy endpoints in depression and anxiety trials is difficult due to the significant placebo effect commonly observed in trials in these patient populations. For example, results from our completed Phase 3 clinical trial of PRX-00023 demonstrated that the product candidate did not achieve a statistically significant improvement over placebo for the primary endpoint with respect to generalized anxiety disorder. Based on these results, we have discontinued our development efforts with respect to PRX-00023 in anxiety and expect to focus our efforts with respect to PRX-00023

in depression. In addition, we must also submit the results of a two-year carcinogenicity study of PRX-00023 prior to its approval. We have not yet initiated this study and intend to conduct this study prior to submitting an NDA to the FDA. If the clinical development of PRX-00023 is delayed as a result of these matters, additional requirements set forth by the FDA, including requirements related to confirming the correct dose for PRX-00023, or otherwise, the time and cost of the development of PRX-00023 could increase significantly.

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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 nine months ended September 30, 2007 was $9.0 million and consisted of $5.0 million of product development revenue from Bayer Schering Pharma AG, Germany, GlaxoSmithKline and CFFT, $0.9 million of royalty revenue related to the Bracco and Bayer Schering Pharma AG, Germany agreements, and $3.1 million of license fee revenue related to the Bayer Schering Pharma AG, Germany, Amgen, Tyco, GlaxoSmithKline and CFFT agreements. In addition to these sources of revenue, we have financed our operations to date through public stock and debt offerings, private sales of equity securities and equipment lease financings.

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

successfully complete our product development efforts;

obtain required regulatory approvals in a timely manner, if at all;

manufacture our product candidates at an acceptable cost and with acceptable quality; or

successfully market any approved products.

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

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

Our product development programs and potential regulatory approval and commercialization of our product candidates will require substantial additional cash to fund expenses. Our strategy includes collaborating with leading pharmaceutical, biotechnology or other companies to assist us in further developing and potentially commercializing our product candidates requiring large commercial sales and marketing infrastructures. We may also seek to enter into such collaborations for our other product candidates, especially for target indications in which the potential collaborator has particular expertise or that involve a large, primary care market that must be served by large sales and marketing organizations. In addition, we depend, and expect to continue to depend, on strategic collaborators for support in a variety of other activities including manufacturing, marketing and distribution of our product candidates in the United States and abroad, if the FDA and corresponding foreign agencies approve our product candidates for marketing. We face significant competition in seeking appropriate collaborators and these collaborations are complex and time-consuming to negotiate and document.

We may not be able to enter into any such collaboration on terms that are acceptable to us, or at all. If that were to occur, we may have to curtail the development of a particular product candidate, reduce or delay one or more of our

development programs or potential commercialization, or increase our expenditures and undertake development or commercialization activities at our own expense. For instance, on July 12, 2006, Bayer Schering Pharma AG, Germany notified us that it decided not to exercise its option to exclusively license EP-2104R, our imaging agent that has completed a Phase 2 clinical trial. As a result, we intend to pursue a collaboration for the continued development of EP-2104R with new potential partners, who may negotiate provisions that allow them to terminate their agreements with us prior to the expiration of the negotiated term under certain circumstances. If we elect to increase our expenditures to fund development, potential regulatory approval or commercialization activities on our own, we will need to obtain additional

capital, which may not be available to us on acceptable terms, or at all. If we do not obtain sufficient funds, we will not be able to complete clinical development of our product candidates or bring our product candidates to market. Further, our receipt of revenues from strategic alliances is affected by the level of efforts of our collaborators. Our collaborators may not devote the resources necessary to complete development and commence marketing of a product candidate in their respective territories, or they may not successfully market product candidates.

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

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

- the limited size of the patient population and the availability of commercial products for certain target indications, including pulmonary arterial hypertension and pulmonary hypertension associated with chronic obstructive pulmonary disease;
- the nature and design of the trial protocol;
- the proximity of patients to clinical sites;
- the availability of other effective treatments for the relevant disease (whether approved or experimental);
- 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.

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

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

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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.

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

Our therapeutic product candidates are currently unformulated.

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

- the current dosage may not provide reproducible amounts of product;
- the pharmaceutical development of a commercially viable formulation may add significant cost and time to our clinical development programs for therapeutics;
- additional trials may be required if the new formulation is not bioequivalent to formulations already used in clinical trials;
- future clinical trials may be delayed in order to identify, develop, optimize, manufacture and certify a commercially viable formulation; and

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

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

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

The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement for marketing our product candidates outside the United States vary greatly from country to country and may

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

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

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

- restrictions on the products, manufacturers or manufacturing processes;
- warning letters;
- civil or criminal penalties;
- fines;
- injunctions;
- product seizures or detentions;
- import bans;
- product recalls and related publicity requirements;
- unanticipated expenditures;

total or partial suspension of production; and

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

The imposition on us of any of the foregoing could materially harm our results of operations. In addition to regulations adopted by the EMEA, the FDA, and other foreign regulatory authorities, we are also subject to